Gastrointestinal Medicine

Symptoms of the GIT diseases

Anorexia: anorexia is loss of appetite. DDx→GIT, Liver, & Malignancies.

Weight loss:

- If the patient is measuring his body weight then a loss of more than 10% in the past 6 months and the patient is not following any diet is considered significant.
- If pt doesn't know about his weight ask about changes in cloths or ring fitness.
- A weight loss of > 0.5 kg/day indicates loss body fluid (not fat) and occurs in diuretic Rx, Sever vomiting or diarrhea, and burn patients.
- About diet ask if the pt is taking any especial diet [e.g. Celiac pt], & if the pt is vegetarian & ask If the pt is taking all of the 3 meals.

Causes of weight loss:

- Inadequate intake, e.g. Depression
- Malabsorption, e.g. Celiac disease
- Disturbed metabolism, e.g. ↑T4 or DM
- Systemic disease, e.g. TB, Malignancy

Weight loss + Good food intake → DM, ↑T4, Malabsorption

Nausea and vomiting

- **Nausea** is the sensation that there is a need to vomit, but without vomiting.
- **Vomiting** is the expulsion of gastric contents via the mouth.

DDx of nausea and vomiting:

1. GIT diseases
2. Drugs (e.g. Chemotherapy, Digoxin, morphine)
3. Systemic diseases (DKA, MI)
4. Pregnancy
5. ↑ Intracranial pressure [e.g. meningitis or brain tumor]

Questions to ask for a patient with vomiting:

1. Time [Onset, Duration, Frequency] • Severity • ↑&↓ Factors • Associated symptoms
2. Amount Smell Color Blood Consistency
3. Projectile or not. [projectile occurs in ↑ICP or in gastric outlet obstruction]
4. Relation to meal
5. In women ask about the last menstrual period

Symptoms of esophageal diseases

- **Dysphagia**: difficulty in swallowing
- **Odynophagia**: pain during swallowing & it indicates the presence of inflammation (e.g. Candidiasis or Herpes simplex infections, or Esophagitis)

Heartburn: retrosternal burning pain due to the presence acids in the esophagus and it indicates GERD

Abdominal pain

Abdominal pain is classified into 3 types: visceral pain, somatic pain, & referred pain.

	Visceral pain	Somatic pain
Nerves	Autonomic (sympathetic)	Somatic (spinal nerves)
Localization	Poorly localized & Midline	Well localized & lateralized
Mechanism	• Distension of hollow organs • Excessive smooth ms contraction	• Irritation of parietal peritoneum
Quality	Constant dull pain or colicky pain	Sharp

In visceral pain the location of pain depends on the embryological origin of the organ:

- **Foregut organs** (esophagus, stomach, duodenum 1st and upper half of 2nd part, liver, biliary tract, gall bladder and pancreas) → **Epigastric pain**
- **Midgut organs** (rest of duodenum, jejunum, ileum, cecum, appendix, ascending colon, and proximal ⅔ of Transverse colon) → **Periumbilical pain**
- **Hindgut organs** (distal ⅓ of Transverse colon, descending colon, sigmoid colon, rectum and upper ½ of anal canal and Genitourinary tract) → **Suprapubic pain**

Referred pain is a pain felt in areas distant from the diseased [e.g. Gall bladder → Right shoulder, Kidney & ureters → Groin and genitalia organ]

Non-alimentary causes of abdominal pain				
CVS & Resp	Neurological	Metabolic	Toxic	Drugs
1. MI 2. Pneumonia 3. Aortic dissection 4. Sickle cell crisis	1. Herpes zoster 2. Tabes dorsalis 3. Spinal cord compression	1. DKA 2. Uremia 3. Porphyria 4. Addison crisis 5. Hypercalcaemia	1. Lead toxicity 2. Spiders bite 3. Snake bites 4. Alcohol	NSAIDs Steroids Iron Digoxin

Abdominal distention

Causes of abdominal distention are flatus, fluid (ascites) and pregnancy.

Jaundice

Definition: *Jaundice* is a yellowish discoloration of the skin, sclerae and mucous membranes and is due to hyperbilirubinemia.

Q. How a pt with bleeding from the GIT presents?

Bleeding from the gastrointestinal (GI) tract may present in five ways:

1. *Hematemesis* is vomiting of red blood or "coffee-grounds" material.
2. *Melena* is black, tarry, sticky, foul-smelling stool.
3. *Hematochezia* is the passage of bright red or maroon blood from the rectum.
4. *Occult GI bleeding* (GIB) may be identified in the absence of obvious bleeding by a fecal occult blood test or the presence of iron deficiency.
5. *Symptoms of anemia.*

Altered bowel habit

- ***Diarrhea*:** is the frequent passage of loose stools of > 3 times every day.
  Another definition is the passage of more than 200 g of stool daily.
  Diarrhea is **chronic** if it lasts more than **2 wk.**
- ***Steatorrhea*** is diarrhea due to fat malabsorption. The stools are pale, bulky and foul-smelling. They float in the toilet pan and are difficult to flush away.
- ***Constipation:*** is the infrequent passage of hard stools of < 1 every 3 days

Questions to ask in patient with diarrhea:

1. Time [Onset, Duration, Frequency] • Severity • ↑&↓ Factors •Associated symptoms
2. Amount Smell Color Blood Consistency
3. Does diarrhea is worse at certain times of the day?
4. Is there any alternating periods of constipation? [Irritable bowel syndrome, Colon cancer, Diverticulitis, Inflammatory bowel syndrome].
5. History of family members or other contacts involvement (school, or work).
6. Ask about the effect of **Fasting** on the diarrhea

↓

Diarrhea can result from impaired water absorption in the colon (**osmotic diarrhea** e.g. malabsorption) or from active intraluminal secretion of fluid due to mucosal inflammation (**secretory diarrhea** e.g. infection, IBD)
Osmotic diarrhea stops if the patient fasts but secretory diarrhea persists

↓

Questions to ask to a pt with constipation:

1. Time [onset, Duration, Frequency] • Severity • ↑&↓ Factors •Associated symptoms
2. Amount Smell Color Blood Consistency
3. Have you noticed periods of constipation alternating with periods of diarrhea?
4. Have you noticed a change in the caliber of the stool?

Causes of diarrhea	Causes of constipation
• Gastroenteritis • Irritable bowel syndrome • Colorectal cancer • Inflammatory bowel disease • Malabsorption • Metabolic [↑T4] • Drugs (antibiotics, iron)	• ↓ high fiber diet • Irritable bowel syndrome • Colorectal cancer • Intestinal obstruction • Immobility (stroke, Parkinson's disease) • Metabolic/endocrine [↓T4, Hypercalcaemia] • Drugs (opioids, iron)

Investigations for GIT

- Plain abdominal-X-ray: it's useful for the diagnosis of intestinal obstruction, perforation, and assessment of pt with IBD

- Bariums studies: name of the barium study depends on the area to be studied:
  - Esophagus → Barium swallow
  - Stomach → Barium meal
  - Small intestine → Barium follow through (the pt drinks barium)
    → Enteroclysis (Small bowel enema)
  - Large intestine → Barium enema

Endoscopy	
Indications of Upper GIT endoscopy	Indications of Colonoscopy
1. Dyspepsia over 55 years of age or with alarm symptoms : o Dysphagia o Vomiting o Weight loss o Acute GI bleeding o Chronic GI bleeding [Fe ↓ anemia] 2. Suspicious barium meal 3. Atypical chest pain 4. Duodenal biopsies in Ix of malabsorption	1. Suspected inflammatory bowel disease 2. Altered bowel habit 3. Rectal bleeding or anaemia 4. Assessment of abnormal barium enema 5. Colorectal cancer screening 6. Colorectal adenoma follow-up 7. Therapeutic procedures
Contraindications	Complication
For Both: 1. Severe shock 2. Recent MI, unstable angina, arrhythmia 3. Severe respiratory disease 4. Possible visceral perforation Upper GIT endoscopy add Atlantoaxial subluxation [As Rheumatoid arthritis pts] Colonoscopy add **Severe active ulcerative colitis**	For Both: 1. Cardiorespiratory depression due to sedation 2. Perforation 3. Bleeding 4. Infective endocarditis Upper GIT endoscopy add aspiration pneumonia

Endoscope: an instrument for examination of the interior of a canal or hollow viscus

Upper GIT endoscopy is also called Esophagogastroduodenoscopy because it can view the esophagus stomach and duodenum

Lower GIT Endoscopy types:
1. **Anoscopy**: allows examination of the distal 6–8 cm of the anus.
2. **Proctoscopy**: measures 15 cm, & used to examine the rectum & distal sigmoid.
3. **Rigid Sigmoidoscopy**: measures 25 cm can see the sigmoid colon.
4. **Flexible Sigmoidoscopy**: measure 60 cm, & reaches up to the splenic flexure.
5. **Colonoscopy**: measure 100–160 cm & used to see the entire colon & terminal ileum

- Scar: Midline, Suprapubic, Lt subcostal, Laparoscopy
- Superficial Veins:
  - Around umbilicus = Caput Medusae (portal hypertension)
  - Lateral veins (SVC or IVC), (check direction of flow, if from up to down it SVC obstruction, if from down to up it is IVF obstruction)
- Skin discoloration: Especially if there are any Scratch marks or Stria

Palpation

- The pt should be asked to place arms at the side of the body
- Ask about the site of the pain
- The pt face should be observed for any expression
- In superficial palpation the examiner's hand should remain in continuous contact with the patient's abdomen
- When palpating for organomegaly never take off your hand until you finish

Aims of Superficial Palpation

1- To be familiar with the patient
2- Tenderness
3- Rigidity (involuntary ms cont)
4- Guarding (voluntary ms cont)
5- For any superficial mass [if pt is asked to contract his ms it becomes less clear]

Deep Palpation

1- Liver
2- Spleen
3- Kidneys
4- Masses

Comment on Palpable LIVER:

- **Size**: normal liver span is < 12 cm
- **Surface**: normally smooth [if irregular: cirrhosis or cancer]
- **Consistency**: Usually firm [Soft in Fatty liver, Hard in Cancer]
- **Tenderness**: tenderness indicates a stretch of its capsule (Glisson's capsule) due to a recent enlargement as in: Acute RVF & Acute hepatitis [Viral or Alcoholic]
- **Pulsation**: pulsatile in tricuspid regurgitation

Causes of **Hepatomegaly** = Causes of **Splenomegaly**

1- Heart failure
2- Liver cirrhosis
3- Malignancy [leukemias, primaries, or secondaries]
4- Infections: Glandular fever [EBV,CMV], Viral hepatitis, and Hydatid disease

Murphy sign: pain on palpation of the right subcostal area during inspiration frequently associated with acute cholecystitis.

Spleen

- Methods to palpate for the spleen:
  1- Normal starting in the Rt iliac fossa
  2- Bimanual exam in Rt lat position

Splenomegaly

- Spleen lies under 9th, 10th, & 11th rib with anterior margin at anterior axillary line
- Sizes: Spleen is palpable if it's 3 times more enlarged than normal
- Not every palpable liver is pathological but any palpable spleen is pathologica
- Massive Splenomegaly is >8cm below costal margin or crosses midline.
  Causes of massive: 1. Myelofibrosis. 2. CML. 3. Malaria. 4. Kala-azar
- Hypersplenism = Splenomegaly + Cytopenia(s) + Hyperplastic bone marrow + response to splenectomy.

Differences between Splenic and Renal mass		
	Spleen	Renal
1-	Cannot get above it	Can get above
2-	Move downward and medially with respiration	No
3-	Notch may be felt	No
4-	No	Ballotable
5-	Dull on percussion	Resonant on percussion

Masses DDx

Right iliac fossa mass	Left iliac fossa mass
1- Carcinoma cecum 2- Crohn's disease 3- Appenicular mass 4- Iliocecal TB 5- Iliac lymphadenopathy 6- Pelvic or transplanted kidney	1- Carcinoma of colon 2- Diverticular 3- Iliac lymphadenopathy 4- Pelvic or transplanted kidney

Epigastric mass	Suprapubic mass
1- Gastric CA 2- Pancreatic pseudocyst 3- Aortic aneurysm (expansile)	1- Bladder 2- Uterus 3- Ovarian cyst

Auscultation

1- Arterial bruit in renal artery stenosis
2- Hepatic bruit in Hepatocellular carcinoma
3- Venous hum in portal hypertension
4- Intestinal sound

Esophageal diseases

Symptoms for Esophageal diseases [Dysphagia, Odynophagia, Heart burn]

Investigations for Esophageal diseases

1. **Barium esophagogram** (Barium swallow): The initial test of choice to evaluate patients with Dysphagia or Suspected esophageal mass lesion.
2. **Esophageal monometery**
   Is used to evaluate the effectiveness of esophageal body and sphincter contractile function. And it used for investigating GERD and Achalasia
3. **Esophageal pH probe monitoring**
   It's used to evaluate the degree of acid reflux into the distal esophagus
   It is the gold standard test for diagnosis of GERD
4. **Esophagoscopy:** It is diagnostic & allows taking of biopsy and may be therapeutic.

Dysphagia

Dysphagia to solids > liquids → Mechanical disorders
Dysphagia to solids & liquids→ Neurological disorders

Mechanical causes of Dysphagia	Neurological causes of Dysphagia
1. Stenosis: • Post GERD • Post-caustic esophagitis • Plummer-Vinson syndrome • Submucosal fibrosis (Schatzki ring) 2. Tumor 3. Pressure from outside: • CA lung • Pharyngeal pouch (Zenker's diverticulum) • Left atrial enlargement in mitral stenosis	1. Achalasia 2. Scleroderma 3. Stroke 4. Bulbar or pseudobulbar palsy 5. Myasthenia Graves (MG) 6. Multiple Sclerosis 7. Amyotrophic lateral sclerosis

Questions to ask to a patient with dysphagia:
1. Is the dysphagia is more to liquids or more to solids.
2. Ask about the level of dysphagia.
3. Is it constant or intermittent

➢ **Plummer-Vinson syndrome = Paterson-Kelley syndrome**:
Female + Esophageal webs→ esophageal stenosis + iron deficiency anemia + atrophic glossitis (these pts has higher risk of postcricoid esophageal cancer)

➢ **Schatzki ring**: Mucosal ring in the lower third of esophagus. Cause is unknown.

➢ **Zenker's diverticulum: a pulsion diverticulum of the mucosa of the pharynx,** just above the cricopharyngeal muscle.

Gastroesophageal Reflux Disease GERD

Definition: GERD is a term used to include pts who suffer with symptoms of reflux, with or without esophagitis or any other complication of acid reflux.

Epidemiology

- GERD affects 30% of the population.
- Male = Female

Pathophysiology: GERD is due to imbalance between defensive factors in esophagus & aggressive factors from the stomach

GERD is due to imbalance between

Defensive factors
- Anatomical Antireflux barriers
- Esophageal acid clearance
- Tissue resistance [squamous]

Aggressive factors
- Intra-abdominal pressure
- Gastric emptying time
- Gastric acidity

- *Anatomical Antireflux barrier*

1. The intrinsic LES (Lower Esophageal Sphincter] tone:
   - LES is located in the distal 4 cm of esophagus and it is tonically contracted and it can prevent reflux even when displaced from the diaphragmatic crura by a hiatal hernia→ that is why not all hernia pt have GERD.
   - Factors → ↓ LES tone → Fatty food, Acidic food [tomato, orange juice], Chocolate
     → Caffeine, Smoking, Alcohol
     → Progesterone
2. Diaphragmatic Rt crus encircle the esophagus & it is an important extrinsic support to the sphincter especially during exercise
3. The intra-abdominal location of the LES.
4. The acute angle of His (oblique entrance of the esophagus into the stomach).

Note: ***Hiatus hernia:*** it is the herniation of stomach into the chest. Hiatus hernia is usually associated with GERD. The hernia causes displacement of the sphincter from diaphragmatic crura with loss of angle of His both will → increase the risk of GERD

- *Esophageal acid clearance:* Normally the presence of gastric acid in the esophagus stimulates peristaltic movement in the esophagus → Removal of reflux material. Pt with GERD have poor esophageal clearance leads to ↑ acid exposure.

- *Delayed gastric emptying* → ↑ in the risk of GERD. It occurs due to Autonomic neuropathy e.g. DM.

- ↑ *in intra-abdominal pressure* [• Obesity • Pregnancy] will ↑ risk of GERD

Clinical picture

Esophageal manifestations:

- Heartburn
- Regurgitation
- Water brash: it is an excessive salivation due to stimulation of the salivary glands by the acids of stomach as a result of regurgitation
- Anemia may occur if recurrent esophageal bleeding is present.

Extra-esophageal manifestations include: [Very Important]

- Cardiac: atypical chest pain which may mimic MI pain even in the response to nitrate, it occurs as a result of spasm due to esophagitis.
- Respiratory: **Reflux-induced Asthma, Ch. cough**, Aspiration pneumonia, Recurrent laryngitis, Pulmonary fibrosis and hiccups
- Others: sudden infant death syndrome and otitis media

Differential diagnosis: It includes the DDx of chest pain, asthma, chronic cough

Investigations

- **Endoscopy with biopsy**:
  - It is helpful in ruling out associated Barrett's esophagus.
  - Erosive changes are seen in only a minority of pts who undergo endoscopy [There is poor correlation between symptoms & endoscopic evidence of esophagitis]
  - Endoscopy Indications: **1.** Age > 55 yr **2.** Symp > 4 wks **3.** Dysphagia **4.** Wt loss
  - If endoscopy is negative consider 24-hr esophageal pH monitoring.
- **24 hour pH monitoring**:
  - A Probe is placed 5 cm above lower esophageal sphincter
  - It's the **Gold standard** test for diagnosis of GERD
  - It Measures the time when the distal esophagus contains gastric acid for 24 hour and the test is positive if pH < 4 for more than 6-7% of the study time.
- Esophageal Manometry. This procedure is useful in evaluating LES pressure.

Complications of GERD

1. Esophagitis ----------
2. Esophageal ulceration ---------- → Upper GIT hemorrhage
3. Benign peptic esophageal stricture → Dysphagia
4. Respiratory complications: Aspiration pneumonia, Asthma, Ch. cough
5. **Barrett's esophagus**
   - It is a condition in which columnar epithelium replaces the normal squamous epithelium of the esophagus (i.e. metaplasia). • It is more common in ♂
   - It is **premalignant state**, with a 40-fold ↑ risk of **adenocarcinoma**.
   - Barrett's is found in **10%** of pts with GERD & **10%** of Barrett's will develop adenocarcinoma

Treatment

- **Dietary and life style modifications**
  - Postural therapy: elevate head of bed; avoid lying down after eating, remain upright at least 2 h after eating (most important life style change)
  - Limit intake of foods and drinks that ↓ LES pressure: fatty food, acidic food (tomato, orange juice), chocolate, caffeine, alcohol. • Stop smoking
  - Avoid medications that ↓ LES pressure: theophylline, nitrates, progesterone, calcium channel blockers, anticholinergic, β-agonists.
  - ↓ the size of the meals • Weight reduction if obese
  - Avoid tight cloths around the abdomen

- **Medical**
  - Antacids [Aluminum-Magnesium compounds] for rapid symptomatic relief:
  - H2-blocker → Rx symptoms but not esophagitis
  - Proton pump inhibitors [given for 4 wks then reduce to minimal effective dose]
    - Most potent single agents and treatment of choice for treating sever reflux esophagitis (e.g. omeprazole, lansoprazole, esomeprazole)
    - Acts by increasing the gastric PH and heal esophagitis
  - Prokinetic agents: Metoclopramide, Domperidone or Erythromycin (act on **motilin receptor**)

- Surgery [Nissen fundoplication]: Laparoscopic or open & it restore the anatomy

Achalasia

Achalasia is the most common esophageal motility disorder.
The term achalasia means "**Failure to relax**"

Pathophysiology

- Due to death of parasympathetic ganglion cells in myenteric plexus (Auerbach's plexus) at the LES → Failure of the LES to relax → ↑ intraluminal pressure → dilatation and eventually loss of peristalsis.
- The cause of death of these ganglion cells is usually idiopathic but it can be secondary to Chaga's disease (*Trypanosoma cruzi*)

Epidemiology

- Commonest in patients between 40 - 70 years
- Male = female

Clinical features

- Symptoms include long history of intermittent dysphagia→ weight loss.
- The dysphagia is for both liquids and solid foods
- Chest pain and regurgitation
- Aspiration of esophageal contents → recurrent pneumonia
- Heart burns does not occur because of hypertonic LES
- 5% of patients develop squamous carcinoma

Investigations

- **CXR**: Widening of mediastinum + air / fluid level and absence of gastric fundus gas bubble
- **Barium Swallow:** Early in disease it may be normal. But later is show dilatation of the distal esophagus with **[Rat tail or Bird's beak]** appearance
- **Manometry** : Hypertonic LES [Gold-standard for Dx of Achalasia]
- **Endoscopy** - essential to exclude carcinoma as a cause of dysphagia

Treatment

1. *Pneumatic Balloon Dilatation*
2. *Cardiomyotomy* (**Heller's operation**)

Esophageal cancers

Epidemiology

- 90% are squamous cell carcinomas & occur in the upper or middle third of the esophagus [The most common site is the Lower third]
- 10% are adenocarcinomas occur in the lower third of the esophagus

Risk factors

➢ *Squamous cell carcinoma*

- Alcohol • Tobacco • Achalasia • Plummer-Vinson syndrome • Celiac Disease
- Diet high in nitrosamines which is found in smoked food
- Aflatoxins which is found in food contaminated with molds
- Post-caustic stricture = Post Lye ingestion • Vitamins A & C ↓.
- **Tylosis** "hyperkeratosis of the palms and soles". A genetic disease (AD) more than 80% of pts develop squamous carcinoma of the esophagus"

➢ *Adenocarcinoma*

- Barrett's esophagus (10% of pts with Barrett's develop adenocarcinoma)

Clinical features

- Progressive Painless dysphagia (more to solids because it's a mechanical cause)
- Aspiration pneumonia or trachea-esophageal fistula → cough of food.
- Nausea & Weight loss
- Some pt develop retrosternal pain as a result of infiltration of mediastinum
- May present with hematemesis and anemia

Investigation

- The investigation of choice is upper gastrointestinal endoscopy with cytology and biopsy (**confirm the diagnosis**)
- Barium Swallow

Management

- Adenocarcinomas are not radiosensitive and surgery is mainstay of treatment
- Squamous cell carcinomas can be treated with either surgery or radiotherapy

Prognosis: Overall 5 year survival is very poor and is at best 10%, And Adenocarcinoma has poorer prognosis than Squamous cell carcinoma

Peptic ulcer disease

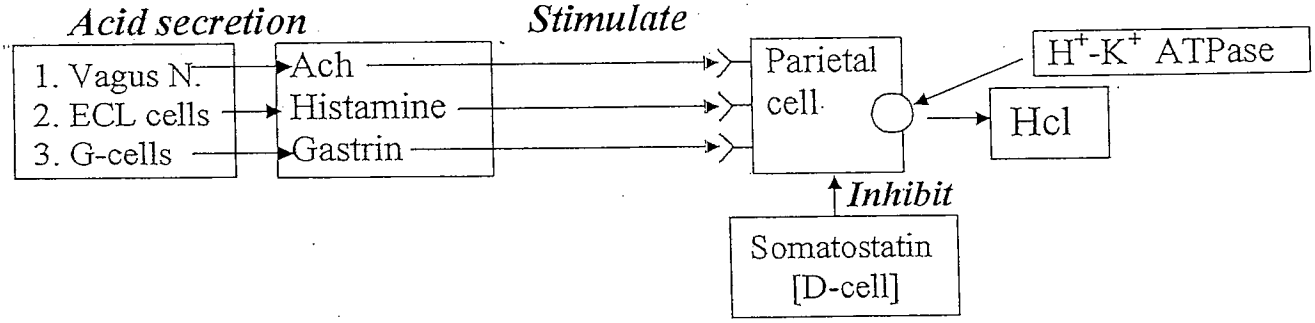
Definition: PU are ulcers that develops only in sites exposed to gastric acid like :

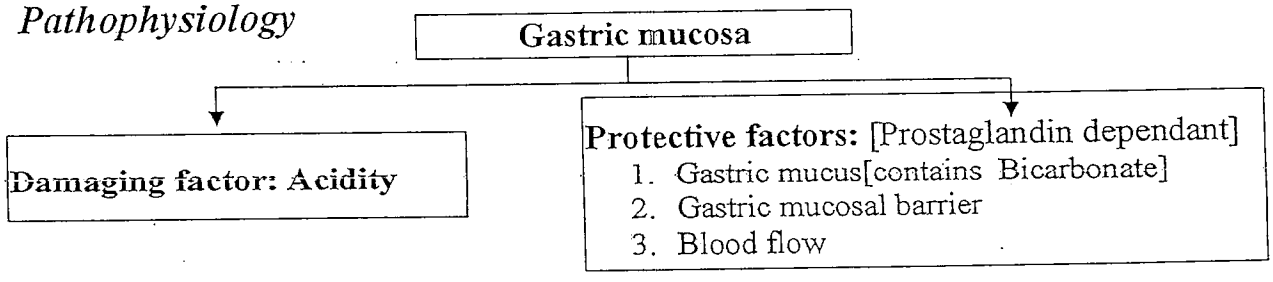
1. Duodenum
2. Stomach, usually antrum
3. Distal esophagus in GERD
4. Jejunum postsurgically after gastro-jejunostomy, or in Zollinger-Ellison syndrome
5. Ileum when there is **Meckel's diverticulum** that contains ectopic gastric mucosa

Etiology and Risk factors [There are 2 major risk factors H. pylori and NSAID]:

1. ***Helicobacter pylori*:** [causes 90% of DU and 70% of GU]
2. **NSAIDs:** [causes 10% of DU and 30% of GU]
3. Gastrinoma [Zollinger-Ellison syndrome].
4. Other risk factors and associations: • [Hereditary , Blood gp O, $\uparrow Ca^{++} \rightarrow \uparrow$ DU]
   • Polycythemia • Mastocytosis • Smoking • Unproven: Stress, Coffee, Alcohol

Helicobacter pylori: A Gram-ve spiral flagellated **Urease-producing** bacteria that Transmits by **fecal-oral or oral-oral routes**. In the gastric mucosa they are extracellular & adherent to epithelial surface hiding in the gastric mucus gel
H. pylori are found in • 90% of DU pts • 70% of GU pts • 60% of gastric CA pts • 50% of people > 50 yrs • 20% of people at 20 ys
Note: H.pylori can invade Only the gastric mucosa (not duodenal)





Peptic ulcer occurs when Damaging factors overcome Protective factors

- H.pylori → Directly damage the gastric mucosa & ↓ Bicarbonate
- NSAID → ↓ Prostaglandins → ↓ Bicarbonate and ↓ Blood flow

How can H.pylori cause DU or GU?

➢ Pathophysiology of GU:

In GU H. pylori infects all of the stomach & causes GU directly by killing gastric cell by toxins [e.g. Vacuolating toxin]. Rates of acid secretion are normal or ↓ in GU pts.

➢ Pathophysiology of DU:

- H.pylori in DU infects the antrum [proximal stomach that secretes Hcl is spared]
- H.pylori damages D-cell → ↓ Somatostatin & stimulates G-cell → ↑ Gastrin –both→ ↑ Hcl (Acid hypersecretion) which directly damage duodenal mucosa + causes gastric metaplasia in the proximal duodenum which allows H. pylori bacteria to colonize the duodenum and produce duodenitis that damages mucosal barrier & ↓ duodenal bicarbonate secretion→ DU.

	Duodenal ulcer	Gastric ulcer
Epidemiology	Duodenal ulcer 3 times > Gastric ulcer Both types are more common in **males** Both are more common in **old age**	
Acid-secretion	Increased	Normal or Decreased
Clinical picture	• **Pain** is **dull** over epigastrium or to Rt of it over the duodenum. • It is **characteristically** relieved by eating & gets worse when stomach empties **[Hunger pain]** • **[Night pain]** pain usually wakes the pt from sleep & is relieved by eating food, drinking milk, or taking antacid. Night pain is due to high nocturnal acid secretion. • **[Periodicity]** The pain episodic with exacerbations for few wks separated by pain-free periods.	• Epigastric pain • Pain usually increases after eating and is relieved by vomiting • Night pain uncommon. • **[Periodicity]**
	• 25% of bleeding peptic ulcers have no history of epigastric pain.	

Differential diagnosis

- Non-ulcer dyspepsia
- GERD: Epigastric pain but mainly when lying flat + burning in the chest ± acid taste in the mouth
- Pancreatitis: Epigastric pain radiating to the back ↑ by eating + ↓ by leaning forwards
- Gallstone pain tends to be colicky and is exacerbated by eating fat.
- Irritable bowel syndrome the pain can occur in the epigastrium and but it extends to the lower abdomen and relieved by defecation.

Investigations

❖ **To Diagnose the ulcer** → Barium meal
→ Endoscopy [Investigation of choice.]

Note: Gastric ulcers may occasionally be malignant and therefore **must always be biopsied AND followed up with endoscopy after 6 wks of treatment to ensure healing.** But Duodenal ulcers biopsy not taken because these ulcers are always benign.

❖ **To Diagnose the cause:**

➢ **NSAID** are diagnosed by history of drug intake

➢ **H.pylori diagnosis**
- **There are many test but Breath tests is the best.**
- Selection of diagnostic test:
  - For pts in whom an endoscopy is clinically indicated for diagnosis or treatment, it is mucosal biopsies for a rapid urease test may be used.
  - For pts in whom endoscopy is not indicated for other clinical reasons, endoscopy **should not** be performed just to diagnose infection with *H. pylori*. a urea breath test or stool antigen should be used.
  - All except serology can give false -ve if the pt has received antibiotics during the past month.

Tests for Detection of *H. pylori*		
Test	Description	Comment
Invasive (Endoscopy/Biopsy required)		
Rapid urease	Color changes due to change in pH	Used when biopsy is done
Histolopathology	Staining of antral biopsies	Takes several days to process
Culture	Difficult culture techniques are needed	Time-consuming, Expensive, Gold standard used only to detect antibiotic susceptibility in refractory cases
Noninvasive		
Serology	By ELISA	Good but **not** useful in follow up because remains +ve for 1 yr after eradication
Urea breath test (^{13}C or ^{14}C breath test)	Ingested radioactive urea is broken down to CO_2	Simple Rapid Highly Sensitive & Specific **Best test for Initial diagnosis** Best test to assess Rx success [**Follow-up**]
Fecal antigen test	By ELISA	Cheap and Accurate

Management

Aims of management → Pain relief by Antacids
→ Healing by inhibiting Hcl secretion [PPI or H_2-blocker]
→ Prevention of recurrence by *H. pylori* eradication with antibiotic

➢ In case of NSAID as a cause:

- Stop NSAID if possible, but if it's necessary to continue NSAID it can be used in combination with either Proton pump inhibitor or Misoprostol

➢ In case of H.pylori as a cause: **Eradication therapy**

- **Eradication therapy** of *H. pylori* markedly reduces rate of ulcer relapse
- The initial treatment for *H. pylori* infection is a **10 to 14days** course of
  Triple therapy → **PPI**
  → **Amoxicillin** [If pt is penicillin sensitive replace with metronidazole]
  → **Clarithromycin**
  This can successfully cure infection in >80% of pts.
  After 14 days antibiotics are stopped and PPI are continued for 1-2 months
- If treatment fails use **Quadruple therapy** → PPI plus
  → Bismuth
  → Tetracycline
  → Metronidazole

Indication for surgery is management of complication:

1. Intractability = Failed medical treatment +
2. Hemorrhage
3. Perforation
4. Obstruction
5. Penetration

Complications

Complications of peptic ulcers:

1. **Hemorrhage** is the most common complication. [More in Posterior wall DU].
2. **Perforation:** 2nd most common complication [More in Anterior wall DU].
   - It leads to peritonitis → severe abdominal pain with board like rigidity and abdomen not moving with respiration.
   - Erect CXR will show air under diaphragm
3. **Gastric outlet obstruction**
   - The narrowing occurs in DU and may be due to edema which resolves without surgery or fibrosis which needs surgery.
   - **C/P**: Abdominal pain + Persisting Vomiting [contains food from previous day] + Constipation. Pts become dehydrated + hypokalemic + metabolic acidosis
   - **Succussion splash** [a noise made by fluid with air when shaken] is present 4 hrs after the last meal.
4. **Penetration** into an adjacent organ usually is a complication of posterior DU, with penetration into the pancreas.

Drugs used in short term management of peptic ulcer				
Group		**Examples**	**Mechanism**	**Comments**
Antacids and alginates		Aluminium- Magnesium compounds +Alginic acid	• Antacids: neutralize acids • Alginates a adheres to ulcer → protective barrier	Aluminium → constipation Magnesium → diarrhea
Anti-secretory	**H_2-Blockers**	Ranitidine Cimetidine	Inhibitors of H_2-receptors on parietal & ECL cells	Cimetidine inhibit warfarin and phenytoin metabolism
Anti-secretory	**Proton pump inhibitors**	Omeprazole Esomeprazole Lansoprazole Pantoprazole	Irreversible inhibitors of H^+/K^+ ATPase on parietal cell surface	**PPI are superior to H_2-blockers** SE: Diarrhea Drug of choice in ZES
Mucosa protection	**Bismuth**		• Adheres to ulcer → protective barrier • **Antimicrobial against *H. pylori***	• Black stool and tongue • Constipation •Neurotoxic
Mucosa protection	**Sucralfate**		• Adheres to ulcer → protective barrier • Very weak antacid • ↑ Epithelial proliferation	Constipation Bezoar formation
Mucosa protection	**Prostaglandin analogues** [Misoprostol]		• ↑ Mucosal blood flow • ↑ Mucus & HCO_3 secretion • ↑ Epithelial proliferation	Diarrhea Abortion [contraindicated in women of child-bearing age]

Zollinger-Ellison syndrome

Definition: Gastrinoma of the pancreas or duodenum → Secret Gastrin → ↑ Hcl→ PU

Epidemiology: • Rare • Age 30-50 yrs • ♂ = ♀

Clinical features:

- Sever peptic ulcer that resist treatment
- Very low pH→ damage pancreatic lipase → Steatorrhea

Dx: **Secretin test:** Normally secretin → ↓ blood gastrin but in ZES it → ↑in gastrin

Rx: If respectable do surgery. If already metastasized PPI are drugs of choice

Diseases associated with H.pylori infection:

1. Peptic ulcer (DU>GU)
2. Chronic gastritis Type B
3. MALToma (mucosa-associated lymphoid tissue) it's **B-cell** lymphoma
4. Gastric carcinoma

Note: there is no relation between H.Pylori and GERD

Gastritis

Definition: Gastritis is the inflammation of the gastric mucosa.

Gastritis is a histological diagnosis and is classified into:

- Acute gastritis—histology→ marked neutrophils with edema and hyperemia
- Chronic gastritis—histology→ cellular infiltrates of lymphocyte and plasma cells

Clinical picture of all types of gastritis:

- Asymptomatic
- Painless upper GIT bleeding → hematemesis and/or melena
- Dyspepsia (epigastric pain) ± anorexia, nausea, or vomiting

Acute (Erosive) gastritis

Pathology→Acute gastritis is often erosive and hemorrhagic.

Causes:

1. NSAID (The **most common** cause for acute gastritis)
2. Heavy Alcohol intake
3. Sever stress:
   a. Burn injury: **Curling ulcer**, an acute gastric ulcer in association with severe burn
   b. Brain injury: **Cushing ulcer**, an acute gastric ulcer in association with head injury
   c. Other causes: (Sepsis, Trauma, Shock, Respiratory, Renal, or Liver failure)

Dx→ Endoscopically, both visually and biopsy

Treatment

- Removal of offending agent
- Antacids: H_2-receptor antagonists, PPI, and Surface-acting agents (sucralfate)

Chronic gastritis

Causes of chronic gastritis:

1. *H. pylori* infection (The **most common** cause for chronic gastritis)
2. Autoimmune gastritis (pernicious anemia) the pt usually have achlorohydria
3. Post-gastrectomy

Dx→ Endoscopically, both visually and biopsy

	Type A gastritis	Type B gastritis
Incidence	Less common	More common
Site	Body-predominant	Antrum-predominant
Cause	Autoimmune	*H. pylori*
CA risk	↑ risk of gastric cancer	↑ risk of gastric cancer & lymphoma
Rx	Corticosteroids	

Gastric tumors

Most gastric tumors are malignant. Most are adenocarcinomas and have a poor prognosis. Less than 5% are malignant lymphomas and these have a better prognosis

Gastric Adenocarcinoma

Epidemiology: More in old age. ♂ > ♀

Pathology

- Adenocarcinomas **most common site** is the **antrum and pylorus** 50% to 60%, and the tumor is more common to occur on the **lesser curvature.**
- Local invasion of gastric carcinoma into duodenum, pancreas, & retroperitoneum is characteristic.
- The most common site for metastasis is the liver.

Risk factors

Precancerous conditions	Genetic and environmental factors
• *H. pylori*	• Family history of gastric cancer
• **Chronic gastritis**	• **Blood group A**
• Adenomatous gastric polyps	• Alcohol
• FAP due to gastric polyps	• Smoking
• Previous partial gastrectomy	• Low socioeconomic status
• **Ménétrier's disease**	• Low consumption of fruits and vegetables
• Barrett's esophagus	• Consumption of salted, smoked food

Clinical picture

- Most tumors present late, commonly with epigastric pain, anorexia and weight loss. The diagnosis should be suspected in any patient with onset of dyspepsia > 55 yrs, particularly if the dyspepsia is associated with any "alarm symptom"
- The pain from a tumor is indistinguishable from that of peptic ulcer.

➢ **Local**

- Epigastric pain
- Dysphagia
- Vomiting (pyloric stenosis)
- Epigastric mass (50%)
- Early satiety
- Hematemesis

➢ **General**

- Anemia: occult GIT bleeding → iron deficiency anemia
- Weight loss is common and suggests advanced metastatic disease

➢ **Metastasis signs**

- Ascites, hepatomegaly, and bone pain
- **Troisier's sign:** palpable Virchow's node (left supraclavicular lymph node)
- **Sister Joseph's nodule:** metastatic nodule at the umbilicus
- **Krukenberg tumor:** secondary ovarian metastasis duo to transcelomic spread

➢ **Paraneoplastic manifestations:**

- Acanthosis nigricans
- Migratory thrombophlebitis (**Trousseau's sign**)
- Dermatomyositis
- Pruritis (**Leser-Trélat sign**)

Investigations

- Barium meal can be useful but it cannot give histopathological confirmation
- **Gastrointestinal endoscopy is the investigation of choice** and should be performed promptly in any dyspeptic patient with 'alarm features'.
- Multiple biopsies from the edge and base of a gastric ulcer are required.
- The tumor may be diffusely infiltrative and called **Linitis plastica** or **Leather-bottle stomach**.
- For assessment of any tumor [CBC, LFT, CXR, Abdominal US] & Abdominal CT for staging

Management

- Because the majority present late, curative resection is not possible for most of the cases. So treatment is palliative surgery or chemotherapy
- If detected early then total gastrectomy can be done
- Palliative chemotherapy can increase quality of life & survival in locally advanced or metastatic disease.
- Of all patients 5 years survival rate is < 30%.
- Radiotherapy is not effective

Acute Upper GIT Bleeding

This is the most common gastrointestinal emergency with annual incidence of 1/1000

Definition: bleeding proximal to the ligament of Treitz.

Causes: *Differential Diagnosis*

- According to the site:
  - Esophagus→ Esophagitis, Peptic ulcer, Tumor, Mallory-Weiss, and Varices
  - Stomach → Gastritis, Peptic ulcer, Tumor, Mallory-Weiss, and Varices
  - Duodenum→ Duodenitis, Peptic ulcer, Aorto-enteric fistula

- *Common causes:* **Peptic ulcer** (Most common) > Mallory-Weiss syndrome > Gastritis, duodenitis. Esophagitis > Varices

Mallory-Weiss syndrome:

- It is a small longitudinal lesions at the gastro-esophageal junction
- It occurs after repeated vomiting and causes a self-limiting bleeding

Clinical picture

- **Hematemesis:** means the vomiting of blood. Blood may be fresh (clots or bright red in color) or altered by gastric acid appearing brown (*Coffee ground*).
- **Melena:** [Tarry black, Offensive, Sticky stool] it is due to degradation of blood to *hematin* by bacteria. It may arise from anywhere proximal to and including the cecum [other causes of black stool: iron or bismuth ingestion but the stool is not offensive].

Melaena is a clinical diagnosis made on the observation of black, tarry, offensive stool on rectal examination or passed spontaneously

- **Hematochezia** refers to passage of bright red blood from the rectum; the blood may or may not be mixed with stool and occurs if the bleeding is heavy.
- If severe bleeding → hypovolemic shock

Clues in History & Examination for the underlying cause:

- **History:**
  - H/O alcohol intake
  - Drug history (e.g. NSAIDs, corticosteroids, anti-coagulants)
  - Normal vomit prior to hematemesis (Mallory Weiss tear, varices)
- **Physical examination**:
  - Look for stigmata of chronic liver disease
  - Presence of telangiectasia on the face and lips or mouth suggest hereditary telangiectasia (**Osler-Weber-Rendu syndrome**) which affects all of the GIT.

Management

- Admission: Pt with Upper GIT bleeding may Re-bleed and re-bleeding has high mortality rate.

- ***Stabilizing the patient (Resuscitation)***
  - Call for HELP
  - Clinical assessment (History and Examination): Vital signs are most important
  - Stabilize the patient ABC
    - A→ Give high-concentration Oxygen
    - B→ Assess breathing by counting the respiratory rate
    - C→ Insert 2 large IV cannula and start infusing fluid and Take blood for:
      - **CBC** (for base line hemoglobin)
      - **Urea** and **Electrolyte**: Urea may be ↑ due to increased protein in the GIT from the digested RBC and due to hypovolemia. $\mathbf{K^+}$ may be ↑ due to absorption of K^+ from digested RBCs.
      - **Blood group** and **Urgent Cross matching** (at least 4 units initially)
      - **Clotting Factors** [PT & PTT should be checked especially in pts on anticoagulants or pts with chronic liver disease]
    - Indications for blood transfusion are:
      - **SHOCK** (Pallor, Systolic BP < 100 mmHg, pulse > 100 bpm)
      - **Hemoglobin < 10g/dl** in patient with recent or active bleeding
    - Continue monitor pulse and BP every half an hour

- ***Identify the source of the bleeding & Treatment***
  - **Endoscopy is the investigation of choice** because its Diagnostic & Therapeutic
  - Endoscopy should be done after adequate resuscitation within 12 hrs of the bleed.

Endoscopic Rx
- Gastritis. Duodenitis. Esophagitis. Mallory-Weiss syndrome → Conservative Rx
- **Peptic ulcer + CA** → Adrenalin injection
  → Heater probe or Laser photocoagulation
- **Varices:** Band ligation or Sclerotherapy or Vasopressin or Sengstaken tube

- Selective arteriography of the celiac artery is used when the bleeding site cannot be identified, usually after 2 or more negative endoscopies.

Drugs that might be used to control bleeding:
- Tranexamic acid [which inhibits fibrinolysis]
- Octreotide [which ↓ acid secretion & splanchnic blood flow]
- Vasopressin is used for variceal bleeding

Poor prognostic factors in Upper GIT bleeding
- Age > 60 years • Re-bleeding • Shock • Co-morbidity: Any organ failure
- Dx: Varices & Malignancy have poorer prognosis [Variceal bleeding Pts have 30% mortality rate at their initial hospitalization & 60% 1-yr mortality rate]

Functional bowel disorders

Functional means **Not organic in origin**; i.e. a disorder with no known or detectable organic basis to explain the symptoms.

Functional bowel disorders:

1. **Globus hystericus**: a feeling of a lump in the throat that need to be swallowed.
2. **Non-ulcer dyspepsia**
3. **Irritable bowel syndrome**
4. **Proctalgia Fugax:** : Painful spasm of anal muscles due to unknown cause

Non-ulcer dyspepsia

Dyspepsia (indigestion): is a *pain or discomfort in the epigastrium* + Belching, Bloating, Early satiety.
Causes of dyspepsia are the same causes of epigastric pain. But when investigations including endoscopy are –ve the condition is called Non-ulcer dyspepsia.

40% of patients who present with persistent dyspepsia have Non-Ulcer dyspepsia

Note: If Pts with pain or discomfort in the epigastrium associated with heartburn the pt should be labeled as gastro-esophageal reflux disease (GERD) and not dyspepsia

Q. What are the indications of Upper GIT endoscopy in patients with dyspepsia?

- Pts > 55 years ± alarm signs
- Pts < 55 years with **Alarm signs**:
    1. Weight loss
    2. Dysphagia
    3. Epigastric mass
    4. Vomiting
    5. Bleeding
    6. Iron deficiency anemia
    7. Suspicious barium meal

Irritable Bowel Syndrome (IBS)

***Definition*:** IBS is an intestinal disorder characterized by chronic abdominal pain and altered bowel habits in the absence of any organic cause = Functional.

Epidemiology

- It is the **Most commonly** diagnosed GIT condition (10% of the population)
- Age→ More common in young [< 40 years]
- Gender→ **Female** > Male

Psychosocial factors → Abnormal bowel Motility → ↑ Peristalsis → Diarrhea; ↓ Peristalsis → Constipation
Psychosocial factors → Abnormal bowel Sensation → Abdominal pain; Bloating

Clinical Picture [Abdominal pain/discomfort + **B**loating + Change in bowel habit]

- The pt is symptom-free for long periods with bouts of symptoms in between
- The **most common** presentation is **Recurrent colicky abdominal pain** [Most commonly in the Lt iliac fossa but can anywhere in the abdomen] and the pain is characteristically **Relieved by defecation**.
- Abdominal bloating = Abdominal distension.
- Altered bowel habits which varies between the patients:
  - Predominantly diarrhea → Low volume stool with mucus but **NO BLOOD**
  - Predominantly constipation → Pellety stools
  - Periods of diarrhea alternating with periods of constipation [**Most common**].

  Patient with IBS present with Diarrhea &/or Constipation
- Associated symptoms include Fibromyalgia, Depression.
- On examination the **only** finding is abdominal tenderness.

Diagnosis: IBS is the Dx of exclusion = All investigation results should be Normal [CBC, ESR, CRP, Barium enema, US, and Endoscopy all are –ve]

The diagnosis of IBS is based on **Rome II criteria**
> **12 wks** [consecutive or not] in the last **12 months** of Abdominal pain + 2 of following: 1. Relieved by defecation 2. Onset associated with changes in stool frequency 3. Onset associated with changes in stool form

Things Do Not occur in IBS:
1. Ac. onset of symptoms
2. Anorexia OR Wt loss
3. Rectal bleeding OR ↓ Hb
4. Nocturnal symptoms

Treatment [Most important step is to reassure the pt].

Treatment depends on the predominant symptoms:

- Diarrhea: Low fiber diet & Anti-diarrheal drugs e.g. codeine
- Constipation: High fiber diet & Laxatives
- Pain/bloating: **Anitspasmodic** (Anticholinergics): Mebeverine , or Peppermint oil
- Low doses of amitriptyline help those with depressive symptoms

Malabsorption

Introduction

Absorption
- **Calcium, Iron, Folic acid** are absorbed in duodenum & upper jejunum
- **Vit-B_{12}** and **bile salts** are absorbed in the terminal ileum
- All other nutrients are absorbed throughout the small intestine

Absorption of fat needs
- Bile salts from the live
- Lipases from the pancreas
- Intact mucosa

→ Disease in any of them → Steatorrhea

- Any cause of steatorrhea will → ADEK vitamins deficiency

Clinical features of Malabsorption = Ch. diarrhea + Wt loss + Abdominal distension

➢ Diarrhea is often steatorrhea [Pale, Bulky, Offensive, Floats in pan & difficult to flush]

Celiac disease = gluten sensitive enteropathy = nontropical sprue

Definition & Etiology:

➢ Celiac disease is an inflammatory disorder of the small intestine due sensitivity to **Gluten** protein [the main antigenic in gluten is **α-gliadin**]

Gluten is found in
- **Wheat**
- **Barley**
- **Rye**

➢ Genetic susceptibility (**HLA B8-DR3**) + Environmental factor (α-gliadin)— for no clear reason→ immune-mediated mucosal inflammation → loss of intestinal mucosal cells → ↓ in absorptive area → malabsorption

Epidemiology

- **Gender**: **Females** > males
- **Age**: Bimodal with a peaks in children [between 6 mo-2yrs] and another peak [between 30-50 yrs] but it may present at any age.
- **Race**: More in Caucasian
- Celiac disease occurs in **10 % of first-degree relatives.**

Pathology

➢ The inflammation → **Loss of villous height** [Villous atrophy] + Thickening of mucosa [Crypt hypertrophy] + inflammatory cells mainly T lymphocyte

➢ The disease is More severe in Proximal small intestine than in terminal ileum

➢ Histological abnormalities returns to normal if the pt eats Gluten-free diet.

DDx of villous atrophy

1. Celiac disease
2. Dermatitis herpetiformis
3. Radiation
4. Lymphoma
5. Zollinger-Ellison syndrome
6. Tropical sprue
7. Whipple's disease
8. AIDS enteropathy
9. Giardiasis
10. Hypogammaglobulinaemia

Clinical presentation

- *In Children*: classically presents soon after weaning when cereals are introduced. The babies usually fail to thrive, refuse to eat, and lose weight. The abdomen becomes distended ± diarrhea [usually steatorrhea]. Abdominal pain, vomiting, Rectal prolapse & clubbing may occur.[Rarely constipation is the major complain].

- *In adults*
  - **Nutritional deficiencies**
    1. **Anemia:** Common & it may be the presenting feature. **[Iron deficiency anemia is most common** > Folate def. > Vit B_{12} def. least common because the terminal ileum is usually spared].
    2. Edema due to hypoproteinamia [Celiac → Protein losing enteropathy]
    3. Vit D deficiency → Rickets in children and Osteomalacia in adults. In severe cases hypocalcaemia which can lead to **tetany**.
    4. Vit K deficiency → Bruises
  - Rarely Classical sprue [Abdominal distension + Diarrhea + Wt loss + Edema]
  - **Dermatitis herpetiformis**: Rare characterized by extremely itchy vesicular rash on the extensor surfaces of limbs, trunk, & scalp. Intestinal symp may be absent.
  - **Clubbing** & **Aphthous ulcers** may occur.
  - **Splenic atrophy** is common.
  - Ataxia due to autoimmune cerebellar degeneration is the commonest neurologic manifestation of celiac disease. Some of pts improve after a gluten-free diet
  - **Associated diseases:**
    - → Type 1 DM.
    - → Autoimmune thyroiditis.
    - → IgA glomerulonephritis
    - → Atopic dermatitis
    - → Selective IgA deficiency is present in 5% of pts

Investigations

- **Immunology:**
  - **Antibodies to α-gliadin**
  - **Anti-endomysial antibody [IgA]** are the **most useful** with a specificity and sensitivity of 90-95%. IgG antibodies must be used in pts with IgA deficiency.
  - **Anti-Tissue transglutinamise antibodies**
- **Hematology:** If Iron def. anemia is present →Microcytic & Hypochromic anemia. If Both Iron + Folate deficiencies are present → **Dimorphic** anemia [meaning that some RBCs are microcytic and some are macrocytic].
  Features of hyposplenism (Heinz bodies & Howell-Jolly bodies) may be seen.
- **Biochemistry:** ± hypoalbuminemia ± hypocalcemia (Vit D deficiency)
- **Intestinal duodenal biopsy** is the **gold standard** for diagnosis. The characteristic features is villous atrophy which resolve when the pt is put on gluten free diet.
- Barium follow-through X-ray: Will show loss of feathery appearance (which reflects the villi) with dilatation of intestine and flocculation of contrast.

Management (Gluten-Free diet for life & replenish deficiencies)

- The main treatment is gluten-free for life which includes:
  - Rice
  - Potatoes
  - Corn (maize)

No Wheat, Rye, Barley, and Oat

- **Note:** Failure of the serum to become negative for the antibody or reappearance of the antibody suggests non-compliance with the diet.
- Dietary supplement may be required in the initial stages of treatment to replenish stores (deficiencies of iron, folate, calcium and/or vitamin D).

Complications

1. T-cell lymphoma of the small intestine (lymphoma complicating celiac disease has poor prognosis). Adherence to a gluten-free diet ↓ the risk of lymphoma.
2. Small-bowel carcinoma
3. Esophageal squamous cell carcinoma

Tropical sprue

Definition: progressive malabsorption in a patient in or from the tropics, associated with abnormalities of small intestinal structure and function.

Etiology → Escherichia coli

Investigation → Intestinal biopsy shows Partial villous atrophy

Clinically → As all malabsorption: ch. diarrhea, abdominal distension, & weight loss.

Treatment → Tetracycline is the drug of choice

Short-Bowel syndrome

Definition: Extensive small intestine resection → ↓ absorptive area → Malabsorption

Etiology: commonest causes of surgical resection [Crohn's disease & bowel infarction]

If terminal ileum is resected → ↓ absorption of Vit B_{12} → Vit B_{12} deficiency
→ ↓ absorption of bile salts → Steatorrhea

Treatment: Dietary supplementation, if fails then TPN (total parentral nutrition)

Whipple's disease

Definition: Rare multi-systemic disorder caused by Tropheryma whippelii infection.

It is more in pts with HLA-B27 +ve and in middle-aged Men

Clinical Features

- Malabsorption: Ch. diarrhea + Wt loss
- **Large-joint arthralgia** • **Lymphadenopathy** • Clubbing • Ataxia

Ix: Intestinal biopsy shows macrophages with Periodic acid-Schiff +ve granules

Management: IV penicillin then oral co-trimoxazole for a year

Blind loop/ Bacterial overgrowth Syndrome

Normally the upper small bowel is sterile due to its high acidity & its peristaltic activity
So Bacterial overgrowth occur if there is:

- ↓ Acidity [Hypochlorhydria] → Pernicious anemia; → Partial gastrectomy; → Partial gastrectomy
- ↓ Peristaltic activity → Scleroderma; → Autonomic neuropathy [DM & Amyloidosis]; → Hypothyroidism
- Structural abnormality → Gastric surgery [**Blind loop** after Billroth II operation]; → Crohn's disease → [Fistula OR Stricture]
- ↓ Immunity: Hypogammaglobulinaemia

Pathophysiology

- The bacteria cleaves bile salts → Steatorrhea
- The bacteria metabolizes Vit B_{12} → Vit B_{12} def. [Folate is produced by bacteria]

Clinical picture: Ch. diarrhea + Wt loss +Abd. Distension + Vit B_{12} def

Investigations

- **[^{14}C]-Glycocholate = Bile salt breath test**: [^{14}C]-bile salts are given orally which when Deconjugated by the bacteria it releases [^{14}C]-CO_2 which measured in breath. In healthy people this occurs in large intestine 4-5 hours after ingestion. But in the small bowel bacterial overgrowth it occurs at 1-2 hrs after ingestion.
- **Hydrogen breath test = Lactulose breath test**: Oral lactulose is given orally which when degraded by the bacteria it releases hydrogen which measured in breath. As [^{14}C]-Glycocholate breath test this occurs earlier than normal people.

Management: Rx the cause. If not possible then Tetracycline is the Rx of choice.

Lactose intolerance

Definition: a disorder in which the pt cannot tolerate lactose due to Lactase enzy. def.
Etiology → Primary; → Secondary [in Celiac pt or Post-Gastroenteritis]
Clinical Features: abdominal discomfort + diarrhea + bloating
Ix: Lactose hydrogen breath test • Stool pH is acidic + Reducing substances in stool
Rx: Avoiding lactose [milk]

Other causes for malabsorption

- **Chronic pancreatitis:** due to ↓ pancreatic lipases
- **Liver** cirrhosis [esp 1ry biliary cirrhosis] → ↓ bile acid → fat malabsorption

Note: Medium-Chain fatty acid can be used as supplement in pt with steatorrhea because they can be absorbed directly without the need of bile salts

Inflammatory Bowel Disease (IBD)

Ulcerative Colitis [UC] **Crohn's Disease [CD]**

Definition: immune-mediated intestinal inflammation due to unknown agent [? bacteria]

Epidemiology

- **Age:** Bimodal occurring in 15–30 yrs & 60–80 yrs
- **Gender:** Male = Female
- **Race:** Jewish > Caucasian > African > Hispanic > Asian
- **Smoking → UC: Smoking** may prevent disease = disease more non & ex-smokers
  → **CD:** Smoking is a risk factor for disease

➢ Others → Appendectomy is protective against UC
→ Oral contraceptive pills increase the risk for CD
→ Crohn's disease is associated with *NOD2* gene

		Ulcerative Colitis	**Crohn's Disease**
Definition		**Diffuse Superficial** inflammation (limited to mucosa & submucosa) that **Always** starts in the **Rectum** & may involve proximal areas but it affects the **Large intestine [ONLY]**	**Localized Transmural** inflammation with non-caseating granulomas and fibrosis that can affect **Any part of the GIT** from mouth to anus
Site		50% → Only Rectum [Proctitis] 30% → Rectum and sigmoid (proctosigmoiditis) 20% → Whole colon (Pancolitis)	40% → Only Small bowel 40% → Small + Large bowels 20% → Only Large bower Most affected site is Terminal ileum
Endoscopy	Ulcers	Superficial with Friable mucosa [bleeds easily]	Deep & Linear [**Cobblestone** appearance]
	Stricture	Rare	Common
	Fistulae	No	Yes
	Pseudopolyp	Yes	No
Biopsy	Inflam.	Superficial, continuous	Transmural, skip lesion/ patchy
	Granulomas	Rare	Majority
	Crypt Abcess	Frequent	Some
	Goblet cells	Depleted	Preserved
Clinical features		Bloody diarrhea & Tenesmus	Abdominal pain & Diarrhea
Pseudopolyps: represent normal residual mucosa between the ulcer			

Clinical features

Course of IBD is relapses and remissions

Acute Exacerbation may be precipitated by → Infections
→ Antibiotics
→ NSAIDs
→ Stress

Crohn's disease

- **Diarrhea** [usually non-bloody] + **Abdominal pain and tenderness**
- Constitutional symptom: Malaise, Anorexia, Weight loss, Fever.
- Vitamins ADEK and Zinc malabsorption may occur.
- Abdominal mass may be found (most commonly at Rt iliac fossa)
- Anal involvement [Anal pain, skin tags, fissures, fistulas, abscesses]
- **Gallstones** [Terminal ileal disease → bile malabsorption → cholesterol supersaturated bile → cholesterol gallstones]
- **Renal Calcium-oxalate stones:** develop due to hyperoxaluria [Normally calcium binds with oxalate → insoluble calcium oxalate, which is eliminated stool. In patients with ileal disease nonabsorbed fatty acids bind calcium and leave oxalate unbound which then is absorbed in the colon].

Ulcerative colitis

- **Bloody diarrhea** [rarely constipation] + **Tenesmus**
- Lower abdominal Cramps (not pain)
- Constitutional symptoms occur less than CD and the anus is usually normal

Toxic Megacolon: a condition where the bowel wall becomes thin & the mucosa is severely ulcerated which may lead to perforation. It is more common in UC than CD

DDx of IBD: → **Infections:** Shigella, Entamoeba histolytica, TB.
→ **Non-infectious:** Diverticulitis, Ischemic colitis, Lymphoma.

Extra-alimentary complications of inflammatory disease				
System	Complication	Ulcerative colitis	Crohn's disease	Response to bowel therapy
Eyes	Uveitis + Episcleritis	+	+	Yes
Skin	**Aphtous ulcers**	+	++	Yes
	Erythema nodosum	+	++	Yes
	Pyoderma gangrenosum	+ +	+	No
Liver	Sclerosing cholangitis	+++	+	No
Ms/Sk	Sacroilitis	+	+	No
	Peripheral arthropathy	+	+	Yes
Other features occurring in both: • **Clubbing** • Amyloidosis • DVT& PE • Erythema multiform • ↑ risk of CA of bile duct **Note:** Most extraintestinal manifestations occur more commonly with UC than or Crohn's colitis than with Crohn's disease confined to the small intestine.				

Investigations

CD & UC may be distinguished Clinically & Endoscopically but histological differences seen on biopsy are the most important.

Laboratory and Radiological:

- In acute exacerbation → Stool examination for parasite & culture for bacteria
  → Plain Abdominal x-ray to look for toxic megacolon
  → ESR & CRP to assess the severity of disease

1. **CBC** [Normocytic normochromic anemia, ↑ WBC, ↑Plt, ↑ESR]
2. **CRP** and Haptoglobin both are useful in monitoring disease activity but ESR is not useful because it takes longer time to reduce after Rx.
3. Antibody tests → P-ANCA is sensitive and found more in UC
   →ASCA is specific and found more in CD
4. Lower GIT Endoscopy & Biopsy → For appearance see table above
   - Sigmoidoscopy can be done in acute disease, but colonoscopy should be avoided
5. Barium Study including Barium follow-through, Enteroclysis, & Barium enema.
   - Barium enema is a less sensitive Ix than colonoscopy
   - Barium is contraindicated in Acute severe disease due to ↑risk of perforation

UC	CD
Barium enema • Loss of haustrations • Superficial ulceration • Pseudopolyps • long standing disease: colon is narrow & short "**drainpipe**" or "**pipe-stem**" colon	Small bowel enema • Narrowing of terminal ileum • Strictures: '**Kantor's string sign**' • Proximal bowel dilation • **Rose thorn** ulcers (deep ulcers) • Fistulae

6. Other investigations → MRI is best for Perianal Crohn's
   →WBC scintigraphy and fistulography may be used in CD.

Management

- It is very important to spend time explaining the disease to the patients.
- The key aims are to →Treat acute attacks [depending on the severity]
  → Prevent relapses
  → Detect carcinoma at an early stage
  → Select patients for surgery

ANY of the following would indicate sever disease

1. Hb < 10
2. Temperature > 38
3. Bloody diarrhea > 6/day
4. ESR > 30 mm/h
5. Pulse > 90 b/m
6. Albumin < 30 g/L

Supportive management

- Rehydration with IV fluids & Correction of any electrolyte abnormality
- Avoid anti-diarrheal drugs & anti-spasmodics because they ↑ the risk of megacolon

Drugs used in IBD

1. *5-Aminosalicylic acid* **[5-ASA]***containing drugs :*

5-ASA is anti-inflammatory drugs used in IBD

- Drugs containing 5-ASA for colonic disease:
  - **Sulfasalazine:** 5-ASA+ Sulfapyridine. It is useful in colonic disease.
  - **Olsalazine** [Olsalazine doesn't cause Azospermia]
  - **Balsazide**
  - Suppositories and enemas of 5-ASA may be used in proctitis.
- Enteric coated drugs (used in Ileocolic disease):
  - **Mesalazine**: enteric-coated tablets with a resin coating is pH-dependent and releases 5-ASA in the ileum and colon.
  - Slow-release mesalazine (**Pentasa**): releases 5-ASA more proximally in the gut; useful in stomach, small bowel and colonic disease.

5-ASA has a role in both active disease and maintenance of remission

Side effects of 5-ASA: Pancreatitis & reversible oligospermia. [not **impotence**]

2. *Glucocorticoids*
   - Orally or as Retention enemas when the disease is localized to the rectum and sigmoid colon. [Severe IBD should be treated with IV steroids]
   - Budesonide is used because it has high topical potency (i.e. causes less side-effects because of poor absorption and rapid first-pass metabolism).
   - Steroids are used in **Active disease** [Steroids have **NO** role in maintenance]

3. *Immunosuppressive Agents*
   - Azathioprine & 6-mercaptopurine used as steroid-sparing drugs
   - Takes 2-4 mo to start acting
   - Has a role in both active disease and maintenance of remission
   - Side effects: Immunosuppression & pancreatitis.
   - All immunosuppressive agents are should be avoided in pregnancy.
4. *Metronidazole:* Used in CD. Side effects:Peripheral neuropathy. Avoid in pregnancy
5. *Inflaximab* (Anti-TNF-α) It's used in CD. Side effects: Flu-like CP & TB in 1/3 of pts

Drugs Rx in Active disease:

1. 5-ASA oral or enema
2. Corticosteroids or Azathioprine or 6-mercaptopurine
3. Metronidazole ± ciprofloxacin in CD

Drug Rx in Maintenance

1. Stop smoking in CD
2. ASA oral
3. Azathioprine or 6-MP
4. Metronidazole ± ciprofloxacin in CD

Rx During Pregnancy & lactation use ONLY Sulphasalazine & Corticosteroids

Management of ***Acute sever IBD***

- NPO, Parentral Rx
- Wait until **7 days** or transverse colon diameter reaches **7 cm** & then surgery is considered. [after 7 days trial with Inflaximab or Cyclosporin is tried before surgery]

Indications for surgery in IBD

- Failed Medical treatment
- Complications (Ac. as Toxic Megacolon perforation) OR (Ch. as Strictures, Fistula)

Complications of IBD

- Toxic megacolon, colonic perforation. [More in UC]
- Cancer [More in UC & screening is recommended to be started after 8 years of the onset of the disease]
- Strictures and Fistulas with CD
- Amyloidosis

Colorectal cancer [CRC]

Epidemiology

- **Age**→ more in elderly
- **Race**→ more in Black
- **Gender**→ • Colonic CA ♂= ♀ •Rectal cancer ♂> ♀
- 80% of cases **Sporadic** (i.e. no family history). • **20% Familial.**

Risk Factors for CA colon

➢ Environmental factors:

- High fiber diet is useful because they contain protective antioxidants + increase stool bulk → ↓ Transit time [time that stool take to move from mouth to anus] → ↓ the exposure of the colon to carcinogens.

↑Risk	↓ Risk
Red meat consumption (Lt colon)	Vegetable (High fiber diet)
Alcohol (Rectal CA)	Folate intake
Smoking	NSAID
↑BMI (Obesity)	High Calcium intake

➢ Diseases and Surgeries that are associated with increased risk:

- IBD (UC > CD) responsible for 1% of cases
- Acromegaly
- Pelvic radiotherapy
- Previous cholecystectomy (Right colon)
- Ureterosigmoidostomy

➢ Polyps:

- Adenomatous Polyps [90% of CRC develop from preexisting adenomas], the malignant potential of adenomas increases with ↑ in size.
- Types of Adenomas: Tubular, Villous [most premalignant], or Mixed.
- The following polyp are not premalignant: **1.** Hyperplastic polyps **2.** Inflammatory polyps **3.** Juvenile polyps **4.** Hamartomatous polyps

➢ Genetics:

❖ Hereditary Non-Polyposis Colorectal cancer HNPCC (**Lynch syndrome**)

- HNPCC is an AD responsible for 10% of CRC cases.
- The risk of colorectal cancer in families with HNPCC is 80%.
- Average age of presentation is at 45 years.
- Amsterdam criteria for diagnosis of HNPCC:
  1. At least three relatives with CRC
  2. The cases span at least two generations
  3. At least one case diagnosed before the age of 50 years

- ❖ Hereditary polyposis syndromes [they are many but Familial adenomatous polyposis (FAP) is the most important]
  - FAP is Autosomal dominant responsible for 1% of CRC cases.
  - FAP typically have hundreds of polyps (adenomas) and are found in the duodenum, stomach and small and large intestine.
  - The risk of colorectal cancer is **100 % by the age of 40 yrs**
  - Adenomas usually begin to develop during the second decade so that screening is started by age of 13 yrs and done yearly thereafter.
  - Most Pts have a total colectomy with ileo-anal pouch in their twenties.

Hereditary cancer syndromes				
Syndrome		GI manifestations	Other clinical features	ALL ARE AUTOSOMAL DOMINANT
Hereditary non-polyposis colon cancer (HNPCC)		Small numbers of colorectal polyps		
Hereditary polyposis syndromes	Familial adenomatous polyposis (FAP)	> 100 adenomas in all GIT	Congenital hypertrophy of retinal pigment epithelium	
	Gardner's syndrome	Colorectal polyps	Osteomas, Desmoid tumurs, Epidermoid cysts	
	Turcot syndrome	Colorectal polyps	Brain tumors	
	Peutz-Jeghers syndrome	Hamartomas in all GIT	Pigmented perioral lesions	
	Familial juvenile polyposis	Juvenile polyps in all GIT	Malrotation. Hydrocephalus	

Clinical presentation

Symptoms of Colorectal cancer according to the site of involvement		
Right side of the colon [Fungating pathology]	Left side of the colon [Annular pathology]	Rectum
Iron deficiency anemia Weight loss Right iliac fossa mass Bowel obstruction is late	**Altered bowel habit** **Lower GI bleeding** Large bowel obstruction	Altered bowel habit Tenesmus Fresh PR bleeding Change stool caliber

- Pain in a pt with colorectal cancer suggests obstructive disease or invasion.
- Weight loss is a late symptom suggestive of advanced disease with poor prognosis.

Examination

- Abdominal examination is often normal but pt may have a mass or hepatomegaly in advanced disease.
- DRE Rectal masses can be detected by digital examination of the anorectal canal.

Investigations (Diagnosis is confirmed with a biopsy)

- **CBC**: may show iron deficiency anemia
- **Barium enema**: does not allow tissue diagnosis
- **Colonoscopy is the investigation of choice.**
- **Search for metastasis (staging):** LFT, Abd CT, and Chest CT.
- **Carcinoembryonic antigen (CEA)**: it is a mucin & it is a tumor marker. It is not useful for diagnosis, but is useful in monitoring the response to treatment and detection of relapse.
- Endoscopic ultrasound & (MRI) may be used to stage rectal cancer

Pathology

Most tumors are adenocarcinomas.

Site: 1/3 occur at the rectum, 1/3 occurs at the sigmoid, and 1/3 occur proximally

Synchronous tumors are present in 2-5% of pts.

Shape of the tumor:

- Polypoid = Fungating = cauliflower
- Annular (apple core)
- Ulcerative

Liver is the commonest site for metastasis

➢ The Dukes' classification for staging of colorectal carcinomas:

The Dukes' classification of colorectal carcinomas			
Stage	Description	% of Pts	5y survival %
Stage A	Involves mucosa or submucosa only	15%	> 90 %
Stage B	Tumor has penetrated the muscle	40%	60 %
Stages C	Lymph node involvement	50%	30 %
Stage D	Distant metastasis		< 3%

- Tumor stage at diagnosis is the most important determinant of prognosis

Screening for colorectal cancer

Screening should begin at age 50 for average risk people and sooner if pt has +ve family history or has IBD

Screening method → Colonoscopy is the best way to prevent & detect colorectal CA
→ Fecal occult blood test every 1-2 yrs ↓ mortality by 16%.

Management

➢ **Surgery:** surgery is required in most cases of colorectal cancer. If possible at least 5cm of normal bowel are resected either side of the tumor, and regional lymph nodes should also be resected. [For right-sided tumors a right hemicolectomy is performed, and a left hemicolectomy for left-sided tumors. Very low rectal tumors are usually treated with abdominoperineal resection of the tumor and rectum.]

➢ **Chemotherapy:** 5-fluorouracil (5-FU) improves survival in Dukes' B & C cancers.

➢ **Radiotherapy:** Preoperative radiotherapy is used for rectal cancer.

➢ **Follow-up:** by colonoscopy and CEA

Hepatology

Anatomy of the liver

The liver divided into left and right lobes by the falciform ligament, but it functionally divided into 8 segments based on its blood supply & biliary drainage & each segment can be removed alone.

Blood supply

- Portal vein → 75% of the total blood supply but only 50% of oxygen supply
- Hepatic artery → 25% of the total blood supply and 50% of oxygen supply
- Sup mesenteric vein + Splenic vein → Portal vein (drains the intestine) + Hepatic artery—Portal tract→ drains into blood sinusoid which is lined by fenestrated endothelium → Central vein → Hepatic vein → Inferior vena cava [IVC]

Cells of the liver

- **Hepatocytes:** constitute 85% of the liver and perform most of the liver functions.
- **Kupffer cells:** lie in the sinusoidal vascular space and represent the largest group of tissue macrophages in the body and are derived from blood monocytes. Its main function is the uptake of bacteria, viruses, and immune-complex.
- **Stellate cells (Ito cell)** lie in the space of Disse Space & it has 2 functions: production of collagen, and storage of vitamin A & D. If Ito cell is abnormally activated "e.g. alcohol" → liver cirrhosis

Functions of the liver

- Synthesis of most important serum proteins [Albumin, Coagulation protein]
- Production of bile and its carriers [Bile acids, Cholesterol]
- Regulation of nutrients [Glucose, Lipids, Amino acids]

Symptoms of liver disease

- **Fatigue** <u>is the most common symptom of liver disease</u>. It is variously described as lethargy, weakness, listlessness, malaise, increased need for sleep, lack of stamina.
- **Nausea, Vomiting, Anorexia**
- **Rt hypochondrial pain:**
  - It occurs due to stretching of **Glisson's capsule**.
  - Causes:
    - → Acute hepatitis [Viral, Alcoholic]
    - → Acute RVF
    - → Liver abscess
    - → Budd-Chiari syndrome.
- **Itching:** It Occurs in cholestatic liver disease [Obstructive Jaundice, PBC & Sclerosing cholangitis] & It may be the presenting symptom
- **Jaundice (icterus):** yellowish discoloration of skin, sclera, & mucous membranes due to accumulation of bilirubin. It is clinically seen when bilirubin > 3 mg/dL

Examination of the liver

Liver size: **Normal liver span is < 12cm** in the right midclavicular line

When liver is palpable how to differentiate between hepatomegaly and ptosed liver?
By percussion to know the liver span **(Normal liver span is <12cm)**

Comment on Palpable LIVER:

- **Size**: normal liver span is < 12 cm
- **Surface**: normally smooth [if irregular: cirrhosis or cancer]
- **Consistency**: Usually firm [Soft in Fatty liver, Hard in Cancer]
- **Tenderness**: tenderness indicates a stretch of its capsule (Glisson's capsule) due to a recent enlargement as in: Acute RVF & Acute hepatitis [Viral or Alcoholic]
- **Pulsation**: pulsatile in tricuspid regurgitation

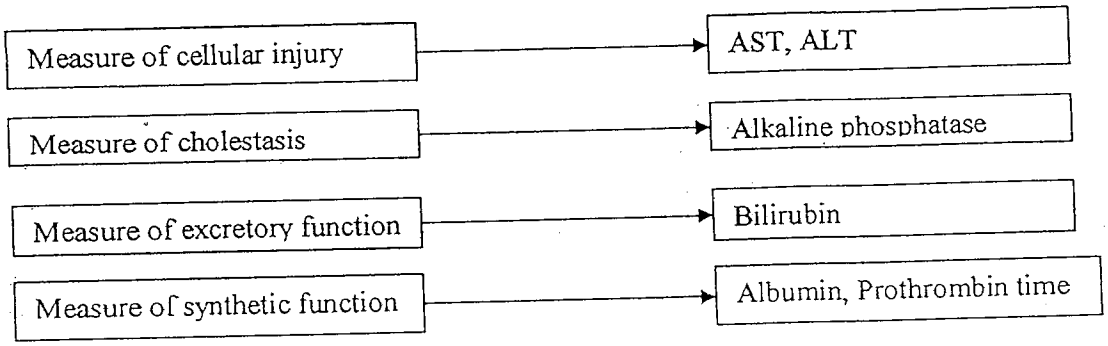
Causes of **Hepatomegaly** = Causes of **Splenomegaly**

1- Heart failure
2- Liver cirrhosis
3- Malignancy [leukemias, primaries, or secondaries]
4- Infections: Glandular fever [EBV, CMV], Viral hepatitis, and Hydatid disease

Investigations for patient with liver disease

A group of 5 blood tests used for initial assessment of liver disease [liver function test]:

1. Serum Aminotransaminases [alanine and aspartate aminotransferases (ALT & AST)]
2. Alkaline phosphatase
3. Serum Bilirubin (direct and total)
4. Albumin
5. Prothrombin time



Serum Aminotransaminases

- Aspartate aminotransaminase (AST) = serum glutamic-oxaloacetic transaminase (SGOT)
- Alanine aminotransaminase (ALT) = serum glutamic-pyruvic transaminase (SGPT)
- Released during hepatocyte plasma membrane damage
- Normal levels of ALT and AST is < **45 IU**, raise of < **6 time** the normal is not specific [i.e. may be cholestatic or hepatitic], but raise of > **6 times** the normal is going with hepatitic liver disease
- AST/ALT > 2 suggests alcoholic liver disease
- ALT is more specific for liver than AST which found in muscles and RBCs.

Alkaline Phosphatase

- Found in Liver, Bone, Intestine, Placenta, Leukocytes
- Normal levels **45–115 U/L**, elevation of < **2.5** time in serum ALP values is not specific but elevation of > **2.5** time in serum ALP occurs in cholestatic liver disease
- Serum ALP should be measured in a fasting state because the level ↑ after a meal
- In biliary obstruction, the bilirubin elevates earlier than ALP.
- The half-life of serum ALP is 7 days.

Bilirubin

- Normal bilirubin levels (0.0–1.0 mg/dL) [1mg = 17 µmol]

Bilirubin production and metabolism:

- Bilirubin is a breakdown product of heme from dead RBCs.
- The formation of bilirubin occurs in the spleen and liver. And the bilirubin formed is insoluble in water and called (**Unconjugated bilirubin**).
- Unconjugated bilirubin binds to albumin to be transported to the liver, where it is taken up by hepatocytes where it is conjugated to glucuronic acid to produce (**Conjugated bilirubin**) which is water soluble.
- The conjugated bilirubin is excreted into bile which drains into the duodenum and passes unchanged through the proximal small bowel. When the conjugated bilirubin reaches the distal ileum and colon, it is hydrolyzed to unconjugated bilirubin by bacterial–glucuronidases to form urobilinogen. About 90% of urobilinogen are excreted in feces and are called stercobilinogen. The remaining 10% of the urobilinogen is absorbed, and enters the portal venous blood, and is reexcreted by the liver. A small fraction escapes hepatic uptake, filters across the renal glomerulus, and is excreted in urine and called urobilinogen.
- So the presence of urobilinogen in urine excludes biliary obstruction as a cause.

Correlation between the level of the bilirubin and the underlying cause:

- In hemolysis unconjugated bilirubin level is < 5 mg/dL
- Bilirubin levels > 20 mg/dL suggest malignant biliary obstruction.

Albumin

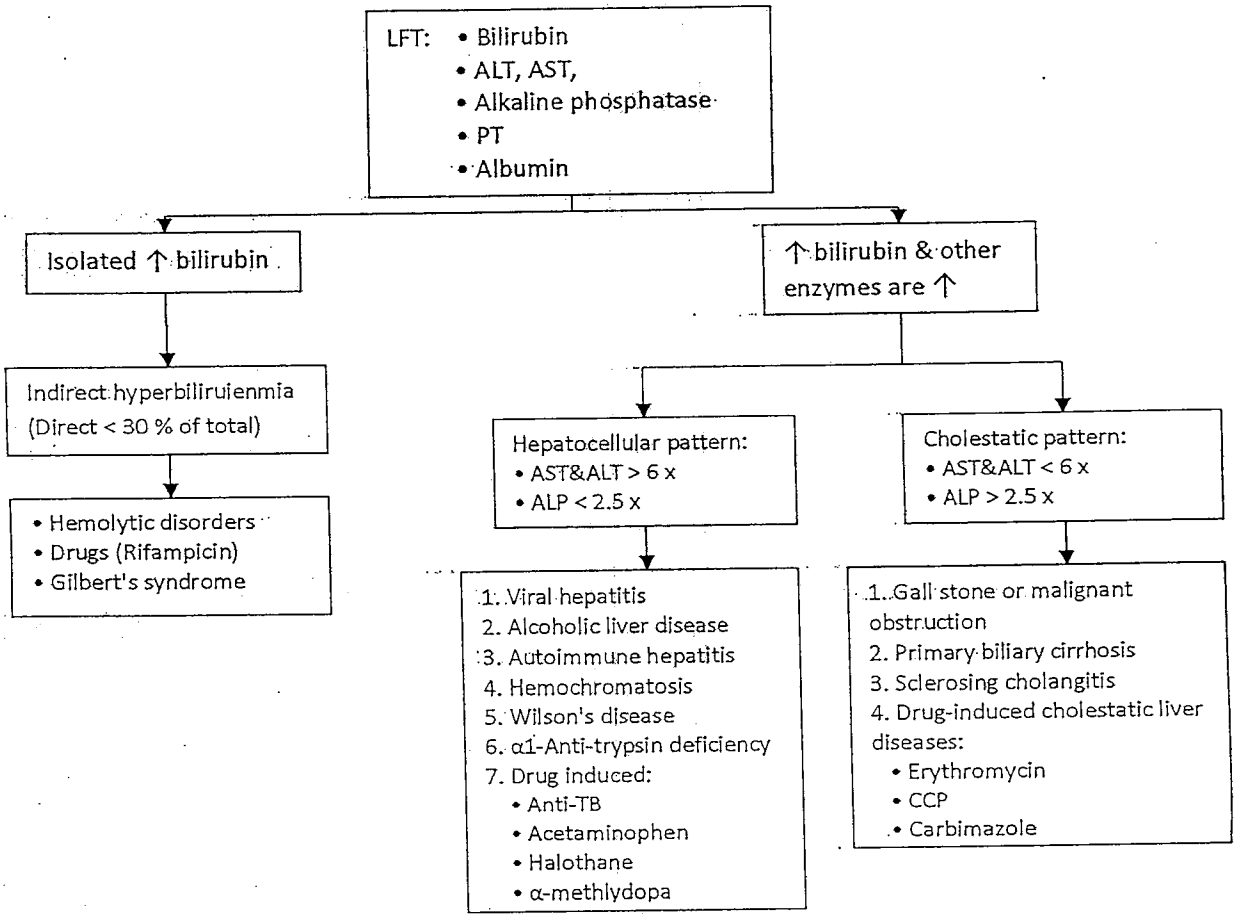
- Most abundant protein synthesized by liver
- Half life = 20 days
- Insensitive to mild injury [**So if Albumin is ↓ = Chronic Sever liver disease**]
- May be affected by nutrition, GIT and renal losses
- When reduced → edema and ascites

Prothrombin Time

- Except for factor VIII, all blood clotting factors are made only in liver.
- The serum half-lives are shorter than albumin [hours] → so it is the single best measure of acute ↓ in hepatic synthetic function.
- Normal PT is (11–13 sec)

Other tests:

- *Gamma-glutamyl Transpeptidase (GGT) + 5'-Nucleatidase* Both are used to determines if elevated ALP is due to liver disease
- *GTT* is also elevated also in Alcoholic pts



Approach to Pt with jaundice

MC: Dark urine & pale stools & itching indicate cholestasis. Dark urine may occur if the cause if hemolysis.

PMHx: Surgery & Anesthesia [halothane], Blood transfusion (hepatitis B or C)

Family Hx: [Hemolytic anemia, Hemochromatosis, Wilson's disease, α1-Anti-trypsin deficiency]

Social Hx: Alcohol, Risk factors for viral hepatitis [Sexual history (A,B,C), Tattoo, Drug abuse], Travel (hepatitis, amoebiasis)

Drug Hx: Anti-TB, Acetaminophen, Oral contraceptive…etc

Jaundice ER → Acetaminophen toxicity
→ Ascending cholangitis [Associated with fever]
→ Fulminant hepatic failure [HBV or Drug induced]

Diagnostic tests in liver disease	
Disease	**Diagnostic Test**
Hepatitis A	Anti-HAV IgM
Hepatitis B	
Acute	HBsAg and anti-HBc IgM
Chronic	HBsAg and HBeAg and/or HBV DNA
Hepatitis C	Anti-HCV and HCV RNA
Hepatitis D (delta)	HBsAg and anti-HDV
Hepatitis E	Anti-HEV
Autoimmune hepatitis	**ANA** (Anti-Nuclear Antibodies) ↑ IgG and biopsy
Primary biliary cirrhosis	**AMA** [Anti-Mitochondrial Antibody], ↑ IgM levels and biopsy
Primary sclerosing cholangitis	**P-ANCA** [Peripheral Antineutrophil Cytoplasmic Antibody], Cholangiography (ERCP) and biopsy
Drug-induced liver disease	History of drug ingestion
Alcoholic liver disease	History of alcohol intake (IgA may be raised) and biopsy
α_{-1} Antitrypsin disease	Reduced α_{-1} antitrypsin levels
Wilson disease	↓ Serum Ceruloplasmin. ↑ Urinary copper. ↑ Liver copper
Hemochromatosis	↑ Serum ferritin + Genetic test for *HFE* gene mutations

Ultrasound uses:

- Biliary duct dilatation and gallbladder stones
- Most sensitive investigation for detecting ascites
- Detecting hepatic masses and liver size
- Directing percutaneous needle biopsies

For Ix for liver mass MRI better than CT which is better than US

Liver biopsy

- Main indication is chronic hepatitis
- Viral hepatitis is not a contraindication

Liver biopsy contraindications	
1. Abnormal clotting (e.g. INR > 1.4)	5. Hydatid cyst
2. Low platelets (e.g. < 60 X 10^9/l)	6. Hemoangioma
3. Anemia	7. Uncooperative patient
4. Bile duct obstruction	8. Ascites

Acute Hepatitis

Viral hepatitis

There are 5 types of viral hepatitis: A, B, C, D, and E. All are hepatotrophic [liver is the primary site of infection]. Other viruses may infect the liver, but it is not their primary site of infection as (CMV), Epstein-Barr virus (EBV), Yellow fever virus.

- Acute hepatitis < 6 months
- Chronic hepatitis > 6 months [**Only** B,C,D virus can lead to chronic hepatitis]

Note: A & E viruses **never** cause chronic hepatitis

Transmission → Parentral transmission (percutaneous, sexual) → A, B, C, D
→ Fecal-oral route in Hepatitis A and E & includes contamination of drinking water and food, and eating raw shellfish

Clinical presentation

- Some pts may acquire infection and remain Asymptomatic
- **All** symptomatic viral hepatitis pts have a similar presentation:
  - After an incubation period depending on the type of the virus the *prodromal symptoms* appear: Anorexia [characteristically severe] Nausea, Vomiting, Malaise, Low grade Fever + Dull upper quadrant pain.
  - The prodromal symptom lasts 3 – 10 days before the onset of *Clinical Jaundice.*
  - Dark urine and clay-colored stools may be found from 1–5 days before the onset of clinical jaundice. The pts starts to feel better after they become jaundiced. The jaundice usually lasts between 2 and 3 wks. But Most pts remain tired for weeks

Investigations

- WBC: normal with a relative lymphocytosis. • ESR: not elevated
- **LFT** → Bilirubin is ↑ and it reflects the degree of liver damage.
→ Prolongation of prothrombin time indicates the severity of the hepatitis
→ Serum aminotransferases (AST and ALT)
  - ↑AST and ALT to > 6x the normal with ↑ of ALP to < 2.5x the normal
  - ALT & AST Level does not correlate with the degree of liver damage
  - Peak levels are usually reached when the patient is clinically jaundiced

Management of acute hepatitis (Symptomatic Rx with Rest and nutrition)

- No specific medications to treat acute hepatitis A and B [only Ac. Hepatitis C **interferon** is used] : Patient with INR > 2 should be admitted.
- Rest [because early exercise after recover is associated with risk of relapse]
- For pruritis: cholestyramine
- No rule for glucocorticoids
- Avoid hepatically metabolized drugs
- Liver transplantation if fulminant hepatic failure & grades III–IV encephalopathy

	HAV	HBV	HCV	HDV	HEV
Viral properties Nucleic Classification	RNA Picornavirus	DNA Hepadnavirus	RNA Flavivirus-like	RNA ----	RNA Calicivirus-like
Incubation	2-6 wks	4-24 wks	2-24 wks	3-20 wks	2-6 wks
Transmission Fecal-oral Percutaneous Sexual Perinatal	 Yes Rare Rare -	 - Yes Yes Yes	 - Yes Uncommon Uncommon	 - Yes Yes Yes	 Yes - - -
Severity Chronic infection/ Carrier Fulminant hepatitis Hepatocellular carcinoma	Usually mild No 0.1 % No	Moderate 10% in adults 70% children 90% in neonates 1% Yes	Mild 80 % Rare Yes	May be severe Common 20% in superinfection ?	Usually mild No 20% in pregnant No
Treatment	None	Interferon + Lamivudine	Interferon + ribavirin	Interferon ±	None
Prophylaxis	Ig Vaccine	HBIg Vaccine	None	None (but HBV vaccine is protective)	None

Hepatitis A virus

Diagnosis IgM anti-HAV which are positive at the onset of symptoms

Management As above

Prevention

After exposure: Immune globulin IM within 2 weeks to household and institutional contacts (not contacts at work). It offers protection for 3-4 months.

Before exposure: inactivated HAV vaccine; given for travelers, military recruits.

Hepatitis B virus (The HBV is also called the Dane particle)

Pt may be Asymptomatic or develop Acute hepatitis & ***Outcome after infection is :***

- Recovery > 90%
- Chronic hepatitis or carrier state < 10% → cirrhosis and hepatocellular CA
- Fulminant hepatitis (<1%)

Note In pts with HBV induced cirrhosis the risk of hepatocellular CA is 5% / yr while pts with HCV induced cirrhosis the risk of hepatocellular CA is 1% / yr. [HBV is more precancerous]

Note: HBV infection: only 10% of HBV infections are chronic versus 80% of HCV are chronic; however, the total number of HBV infections is much greater than HCV.

Interpretation of HBV serologic marker	
Hepatitis B surface antigen [HbsAg]	HBV infection: Acute or Chronic
Hepatitis B e antigen	High levels of HBV replication & infectivity
Anti-HBe	Low levels of HBV replication & infectivity
Anti-HBc (IgM)	Recent HBV infection
Anti-HBc (IgG)	Recovered or chronic HBV infection
Anti-HBs	Immunity to HBV infection
Anti-HBc (IgG) + Anti-HBs	Past HBV infection
Anti-HBc (IgG) + HBsAg	Chronic HBV infection

Extrahepatic manifestations: **Polyarteritis nodosa,** Aplastic anemia (rare),Rash, Urticaria, Arthritis, Neuropathy, Glomerulonephritis.

Treatment

- Acute: as HAV **[no antiviral therapy]**
- Chronic: interferon ± (standard and pegylated), lamivudine, adefovir, &entecavir.

Prevention

After exposure: Hepatitis B immune globulins (HBIg) IM immediately after needle stick, within 14 days of sexual exposure, or at birth (HbsAg+ mother).

Before exposure: Recombinant hepatitis B vaccine IM at 0, 1, & 6 months, given in deltoid injection.

Hepatitis D virus

Defective RNA virus that requires HBV for its replication; either co-infects with HBV or superinfects a chronic HBV carrier.
HDV ↑ the severity of HBV infection (acceleration of ch. hepatitis to cirrhosis).
Diagnosis Anti-HDV in serum
Prevention Hepatitis B vaccine.

Hepatitis C virus

Note: Hepatitis C virus infection is the most common transfusion transmitted infection

Most Pt are Asymptomatic [Acute hepatitis is rare] & ***Outcome after infection is :***

- Recovery <20 %
- Chronic hepatitis or carrier state > 80% → cirrhosis and hepatocellular CA
- Fulminant hepatitis (<1%)

Note: Ch. hepatitis C → cirrhosis in 20% of pts after 20 yrs

Diagnosis

- Anti-HCV in serum (serologic test) may appear after acute illness but generally present by 3–5 months after exposure.
- A positive Anti-HCV test should be confirmed by detection of HCV RNA in serum by PCR due to of false-positive results that may occur.

Extrahepatic manifestations: **Essential mixed cryoglobulinemia**, **Porphyria cutanea tarda**, Glomerulonephritis, and lymphocytic sialadenitis.

Treatment

- Acute: As HAV + **interferon** because it's effective reducing the rate of chronicity
- Chronic: Rx of choice : sustained release (PEGylated) interferon-α + Ribavirin. Antiviral therapy leads to 60% sustained response (viral clearance).

Pts with good response to IFN are:

1. Favorable genotype (genotypes 2 & 3 **not** genotypes 1 & 4)
2. Low baseline HCV RNA
3. Histologically mild hepatitis with minimal fibrosis
4. Age <40 years
5. Absence of obesity
6. Female gender

Prevention Exclusion of paid blood donors, testing of donated blood for anti-HCV. There is no vaccine for hepatitis C

Alcoholic liver disease

Three forms of liver diseases that may occur due to alcohol consumption:

1. **Fatty liver:** occurs in 50% of heavy drinkers, & is reversible on alcohol cessation
2. **Acute Alcoholic hepatitis:** occurs in 40% of heavy drinkers.
3. **Cirrhosis:** occurs 10% of heavy drinkers.

Alcoholic liver disease is associated with ingestion of 160 g/d for ♂ and 110 g/d for ♀ for >8 years; [♀ higher risk is due to ↑ gastric & hepatic metabolism of alcohol]
Factors that ↑alcohol toxicity: • Undernutrition and obesity • Hepatitis B and C

Clinical presentation

➢ **Fatty Liver**

- May follow even brief periods of ethanol use.
- Its **asymptomatic hepatomegaly** and mild elevations in biochemical liver tests.
- Reverses on withdrawal of ethanol; does not lead to cirrhosis

➢ **Alcoholic hepatitis**

Alcoholic hepatitis is an acute illness associated with acute or chronic alcohol abuse.
Patients present with:

- Deep jaundice
- Right upper quadrant pain with tender hepatomegaly
- Fever
- ↑ WBC • ↑ INR

Management is supportive + **glucocorticoids**

➢ **Cirrhosis:** Dupytren's contractures, palmar erythema & parotid enlargement are more common in alcoholic cirrhosis.

Investigations (Recognition of alcohol abuse) hypertension +

- **CBC**: **Macrocytosis** in the absence of anemia
- **LFT**: [Both AST and GGT are induced by alcohol]
  - AST/ALT ratio is > 2
  - ↑ GGT
- ↑ uric acid
- Alcohol → Frequent falls → Unexplained rib fractures on **CXR**

Management: Stop alcohol

Non-alcoholic steatohepatitis [NASH] = Fatty liver : it is a term used to describe liver changes similar to those seen in alcoholic hepatitis in the absence of a history of alcohol abuse. It is common. And it is the Dx of Exclusion

Associated factors	Clinical presentation
• Obesity • Type 2 diabetes mellitus • Sudden weight loss	• Asymptomatic • Hepatomegaly ALT is typically greater than AST

Drug induce liver disease

Drug-induced hepatitis	Drugs-induced cholestasis	Drug causing cirrhosis
1. Paracetamol 2. NSAID 3. Anti-TB drugs 4. Halothane 5. Na-Valproate, phenytoin 6. Statins 7. MAOIs 8. Methyldopa	1. Anabolic steroids 2. Contraceptive pills 3. Chlorpromazine 4. Antibiotics: • Flucloxacillin • Co-amoxiclav • Erythromycin • Nitrofurantoin	1. Methotrexate 2. Methyldopa 3. Amiodarone

Paracetamol poisoning

For paracetamol, 12 g (24 tablets) is potentially fatal dose in most patients, where as 7.5 g (15 tablets) may be lethal in high-risk individuals. [e.g. alcoholics, HIV]
Most cases of paracetamol poisoning are intentional and constitute a suicide attempt.
Paracetamol poisoning can cause liver failure and occasionally renal failure.

Clinical picture

Stage	Time after ingestion	Clinical presentation
1	30 min-24 hours	**Asymptomatic**, or vomiting and diarrhea
2	24-72 hours	**Gastrointestinal symptoms resolve**; at 36 hours, liver transaminases begin to ↑
3	72-96 hours	Hepatic necrosis, Jaundice, Hypoglycemia, Lactic acidosis, Encephalopathy, Coagulopathy, Renal failure
4	4days-2 weeks	Recovery, or progressive liver damage or death

Management

1. **Gastric lavage:** is done if the patient presents to hospital within 4 hours of ingestion and has taken at least 15 tablets.
2. **Activated charcoal:** is given If a patient presents within 1 hour of ingestion
3. Obtain serum acetaminophen level 2-4 hours after ingestion. Level should be plotted on the **Matthew-Rumack nomogram** to determine potential for hepatitis
4. **Intravenous N-acetylcysteine** is antidote of choice it is most protective if given within 8 hours. But it may be still helpful up to 72 hours after ingestion
5. **If** the patient present 16 hours or more after ingestion, treatment should be started as soon as possible & serum concentration is no longer useful guide for diagnosis.
6. The assessment of liver damage can be made by:
   - Serial INR
   - Liver enzymes

Chronic liver diseases

Etiology

- **Hepatocellular**: HBV and HCV chronic infections, Hemochromatosis, Wilson's disease, α1-antitrypsin deficiency, and Autoimmune hepatitis.
- **Cholestatic**: Primary biliary cirrhosis, and Sclerosing cholangitis.

Hemochromatosis

Definition: It is **primary** iron overload (Total body iron of > 5 g) (Normal is < 3 g).

Epidemiology

- Age: About 40 yrs
- Associated with HLA-A3
- Gender: ♂ > ♀ 9:1 [because iron loss in menstruation & pregnancy is protective]

Pathophysiology & Clinical picture

Hemochromatosis is an **Autosomal Recessive** disease in which there is a mutation in the **HEF gene** –not clear how→ increased GIT absorption of iron and then excess iron is deposited in to:

- Liver → Hepatomegaly, Cirrhosis and Hepatocellular carcinoma
- Pancreas → Diabetes in $^2/_3$ of pts
- Heart→ Restrictive cardiomyopathy → Heart failure
- Joints→ Osteoarthritis
- Skin → Bronzed appearance [due to ↑ melanin deposition]
- Endocrine glands → Hypogonadism, Gynecomastia

With Exception of DM all other symptoms improve on Rx

Note: In Hemosiderosis there is abnormal accumulation of iron but no cell destruction. But in Hemochromatosis there is abnormal accumulation of iron with cell destruction]

Investigations

- **LFT:** non-specific hepatitis, and may be normal.
- **Iron indices**: Elevated iron saturation and Serum ferritin.
- **Genetic test:** *HFE* gene mutations.
- **Liver biopsy:** confirms Dx by showing iron stores.

Management

- **Venesection:** 500 g of blood removed weekly until excess iron stores removed (which may takes up to 18 months)
- **Surveillance for hepatoma** by α-fetoprotein and ultrasound in cirrhotic pts because it occur in $^1/_3$ of pt even after treatment
- **Screening of first-degree relatives:** by the HEF gene analysis
- Liver transplantation if end-stage liver disease

Note: Secondary hemochromatosis is increased intake and accumulation of iron secondary to known cause, e.g. multiple transfusions in Thalassemia.

Wilson's disease

Definition

Wilson's disease is an **Autosomal recessive** disorder characterised by excessive copper deposition in the tissues.

Pathophysiology

Defect in the **ATP7B gene** located on chromosome 13 which is coding for copper transport protein → ↑ copper absorption from small intestine & ↓ hepatic copper excretion into the bile.

Clinical presentation

The onset of symptoms is usually between 10 - 25 yrs. Children usually present with liver disease while young adults often present with neurological disease

Features result from excessive copper deposition in the tissues, especially the brain, liver, cornea, and kidney:

1. **Hepatic**: Acute hepatitis (rare), chronic hepatitis, and cirrhosis.
2. **Neurological**: Speech and behavioral problems + Extrapyramidal disturbance: tremor, chorea. The neurological disease is permanent.
3. **Kayser-Fleischer rings** (due to deposition in the cornea)
4. **Hemolytic anemia** (due to spillage of copper into the blood)
5. Blue nails & Renal tubular acidosis (Fanconi syndrome)

Diagnosis

- **Copper study**: ↓ serum ceruloplasmin (transport protein) →↓ serum total copper, (but there is ↑ in free copper in blood) and ↑ 24hr urinary copper excretion
- **Liver biopsy**: Confirms Dx
- **Brain CT or MRI**

Management

- **D-penicillamine** [Chelating agent] is the drug of choice. Zinc may be used.
- **Screening of first-degree relatives**
- Liver transplantation if end-stage liver disease

Deficiency of α1-antitrypsin

Deficiency of α1-antitrypsin is rare genetic disorder in which the enzyme produced by the pt is abnormal → Accumulates in the liver → **Chronic liver disease**
↳ ↓ α1-antitrypsin → **Emphysema** especially in smokers.

Dx: ↓ levels of α_{-1} antitrypsin in serum
Rx: There is no specific treatment.

Autoimmune hepatitis *(Lupoid hepatitis, or plasma cell hepatitis)*

Definition: An autoimmune disease affecting the liver due to unknown etiology

Epidemiology

- *Age:* 30-50 years
- *Gender:* ♀

Clinical presentation

- Acute hepatitis in ⅓of pts: present as viral hepatitis
- Chronic hepatitis in ⅔ of pts:
  - Fatigue, Anorexia, Fever Jaundice, Hepatomegaly.
  - Other features: **Amenorrhea**. Acne, Stria.
  - Stigmata of Ch. liver disease

Extrahepatic manifestations: Rash, Arthralgia, Keratoconjunctivitis sicca, Autoimmune hemolytic anemia.

Associated diseases: 1. Ulcerative colitis 2. Thyroiditis 3. ILD

Investigations

- LFT: shows a hepatocellular pattern
- Antibodies:
  - Antinuclear antibody [ANA]
  - Smooth-muscle antibody [SMA]
  - Anti-liver/kidney microsomal [anti-LKM] antibodies.
- Hypergammaglobulinemia = ↑IgG (100%)
- Other test: False +ve Rheumatoid factor & Anti-HCV enzyme immunoassay
- Liver biopsy: confirm Dx if in doubt

Treatment

- **Immunosuppression**
  - Acute autoimmune hepatitis is very sensitive to high-dose steroids.
  - Longer term management is by steroid ± azathioprine **improves survival**
- Liver transplantation if end-stage liver disease

Prognosis

If no treatment 50% of pts will die within 5 years but with treatment it falls to 10%.

Primary biliary cirrhosis

Definition: It is a chronic cholestatic liver disease in which the intrahepatic biliary cells are damaged by an autoimmune process → progressive cholestasis → cirrhosis.

Epidemiology

- Age: 30-50 years
- Gender: More in ♀ (female: male ratio of 9:1)
- Smoking is a risk factor
- Associated disease include: Sicca syndrome, ILD.

Clinical (classic presentation is itching in a middle-aged woman)

- Asymptomatic & diagnosed by incidental finding of ↑ ALP on routine LFTs
- **Typical** presentation is with **pruritis** [most common initial complaint and is due to retention of bile salts] followed by the appearance of jaundice.
- ↓Bile salt → steatorrhea which may → fat soluble vitamins (ADEK) deficiency.
- **Hyperpigmentation**, especially over pressure points (due to bile salts deposition)
- **Xanthomas** & Xanthelasma (especially around the eyes)
- Clinical features of Cirrhosis (hepatomegaly, splenomegaly, clubbing…)

Investigations

- **LFT:** shows cholestatic picture (ALP > 2.5x the normal)
- Anti-mitochondrial antibodies (**AMA**) M_2 is highly specific
- Raised serum IgM
- Hypercholesterolaemia is common
- **Liver imaging:** ultrasound (to exclude stones, and sclerosing cholangitis)
- **Liver biopsy:** only if the diagnosis is in doubt

Management

- Pruritis: Cholestyramine
- **Ursodeoxycholic acid** slows the progression of the disease & improves LFT
- Fat-soluble vitamin supplementation
- Liver transplantation if end-stage liver disease (PBC is a common indication)

Note: Secondary biliary cirrhosis: occurs 2ndry to prolonged obstruction of the bile duct (stones, stricture, tumor)

Primary sclerosing cholangitis [PSC]

- PSC is a biliary disease of unknown etiology characterised by inflammation and fibrosis of intra and extra-hepatic bile duct. It is associated with UC & HIV
- 5% of pts with UC have PSC & 80% of patients with PSC have UC

Clinical feature: Cholestasis = mainly pruritis

Ix: **ERCP** shows multiple biliary strictures giving a **Beaded** appearance •**P-ANCA** +ve

Complications: • Cholangiocarcinoma (in 10%) • ↑ risk of colorectal cancer

Liver Cirrhosis

Definition: A disease of the liver that is characterized by fibrosis, disorganization of the lobular and vascular architecture, and regenerating nodules of hepatocytes.
Cirrhosis = Fibrosis + Disorganization of structure + Regeneration nodule

Etiology

- Viral hepatitis (B, C, D) [most common cause in unde[illegible]world]
- Alcoholic liver disease [most common cause in Western wo[illegible]
- Primary biliary cirrhosis
- Primary hemochromatosis
- Wilson disease Rare
- α_1-Antitrypsin deficiency Rare
- CHF (Cardiac cirrhosis)
- Cryptogenic cirrhosis 10%

Clinical presentation

Symptoms
Anorexia, Nausea, Vomiting, Diarrhea, Fatigue, Jaundice, Amenorrhea, Impotence.

Signs: Early Hepatomegaly but Late in the disease the liver becomes shrunken.

Signs of Chronic liver disease in GE	
Site	Signs
Hands	Clubbing, Leukonychia, Terry's nail, Palmar Erythema, Dupuytren's contracture, Spider naevi, Liver flap
Face	Telangiectasia, Spider naevi, Parotid enlargment, Jaundice, Pigmentation, Central cyanosis
LL	Ankle edema
Trunk	Gynecomastia, Excoriation

Leukonychia: mean white nails and it occurs in hypoalbuminemia which occurs in liver disease, nephrotic syndrome and malnutrition.

Dupuytren's contracture: thickening & shortening of the palmar fascia → flexion deformities, particularly of the little and ring fingers. [More in alcoholic liver disease]

Spider angiomata: a telangiectatic arteriole in the skin with radiating capillary branches simulating the legs of a spider; Spider naevi of > 5 is pathological. They may occur also in pregnancy.

Hepatic failure: Clinical picture hepatic encephalopathy OR Ascites in pt with severe acute or chronic liver disease
Note: Spider angiomata & Palmar erythema occur in both Acute & Chronic liver disease
Note: Signs of advanced liver disease include muscle-wasting, ascites, and edema

Investigations

- **CBC:** Anemia (microcytic due to blood loss), Pancytopenia (hypersplenism).
- **RBS**: may show hypoglycemia.
- **Coagulation test:** Prolonged PT.
- **Urea and electrolyte:** hyponatremia.
- **ABG**: hypokalemic alkalosis, hypoxemia (hepatopulmonary syndrome).
- **Blood protein**: hypoalbuminemia (albumin level < 3.5 g).
- **Liver biopsy** is the gold standard for the Dx of cirrhosis, but the Dx is usually made on C/P & Other investigations & biopsy is done for difficult cases only

Morphology → Macronodular > 3mm → Post-hepatitis
Morphology → Micronodular < 3 mm → Alcoholic + Hemochromatosis

- For Diagnostic test of the cause see (page 7)

Complications

1. Portal hypertension → Ascites which may → Spontaneous bacterial peritonitis
   → Esophageal varices
   → Splenomegaly which may → Pancytopenia
2. Systemic effects → Hepatic encephalopathy
   → Hepatorenal syndrome
   → Hepatopulmonary syndrome
3. Others → Bleeding tendency
   → Malnutrition
   → Hepatocellular carcinoma

Prognosis

Child-Pugh Classification of Cirrhosis				
Factor	**Units**	**1**	**2**	**3**
Serum bilirubin	mol/L	< 35	35-51	>51
Serum albumin	mg/L	> 35	30-35	<30
INR		<1.7	1.7-2.2	>2.2
Ascites		None	Controlled	Poorly controlled
Hepatic encephalopathy		None	Minimal	advanced

Child-Pugh classification with a scoring system of 5–15:

- Class A (score of ≤ 6): Compensated cirrhosis.
- Class B (scores of 7–9): Decompensated cirrhosis.
- Class C (scores of 10–15): End-stage liver disease [life expectancy 1-3 months]

Uses of Child-Pugh:

1. Reliable predictor of survival in liver diseases (i.e. prognosis in cirrhosis)
2. Predicts the risk complications of cirrhosis such as bleeding from varices.
3. If pt is in Class B it is an indication for liver transplantation

Portal hypertension

Definition: Portal vein pressure >10-12 mmHg. [Normal < 10 mmHg]

Clinical features

Increased portal pressure will result in the following:

1. Increased collateral circulation between high pressure portal venous system & low-pressure systemic venous system in sites of portosystemic shunts which are:
   - Lower esophagus & upper stomach → Varices
   - Rectum → Hemorrhoids
   - Anterior abdominal wall → Caput medusae [Bl. flows away from umbilicus]
   - Note: portosystemic shunting is a risk factor for hepatic encephalopathy
2. Ascites
3. Splenomegaly ± hypersplenism

Rx : Propranolol

Other causes of Portal Hypertension:

- **Budd-Chiari syndrome** = Hepatic vein thrombosis: the condition is associated with hypercoagulable states. Pts usually have ascites. Dx is by Doppler ultrasound Rx is by transjugular intrahepatic portosystemic shunt (TIPS) placement.
- **Splenic vein thrombosis**
- **Schistosomiasis**

Esophageal varices

Clinically presents as Upper GIT bleeding

Investigation: Upper GIT Endoscopy is the Ix of choice.

Treatment

- Primary prevention of variceal bleeding is by **Propranolol** (portal venous antihypertensives)
- Treatment of variceal hemorrhage
  - ABC
  - Correct clotting: FFP, Vitamin K
  1. Endoscopic band ligation or sclerotherapy is the **Procedure of choice**; banding is better than sclerotherapy.
  2. Medical treatment [used only in active bleeding] they ↓ portal blood flow by causing splanchnic arterial vasoconstriction:
     a. Terlipressin (Vasopressin) has shown to ↓ mortality and it is used with nitroglycerin to prevent coronary & renal vasoconstriction
     b. Octreotide (Somatostatin analog) used when Terlipressin is contraindicated
  3. Sengstaken-Blakemore tube if uncontrolled hemorrhage
  4. Transjugular Intrahepatic Portosystemic Shunt (TIPS) if above measures fail

Hepatic Encephalopathy

Definition: A state of disordered CNS function associated with severe acute or chronic liver disease; may be acute and reversible or chronic and progressive. There is a characteristic EEG abnormality which correlate with clinical stage.

Clinical presentation

Stage 1: euphoria or depression, mild confusion, slurred speech, disordered sleep (cycle reversal)
Stage 2: lethargy, moderate confusion.
Stage 3: marked confusion, sleeping but arousable, inarticulate speech.
Stage 4: coma; initially responsive to noxious stimuli, later unresponsive.

Sign: Flapping tremor are present unless the pt is unconscious. Fetor hepaticus

Pathophysiology

- Failure of liver to detoxify agents harmful to CNS e.g. Ammonia, GABA, Mercaptan, Fatty acids.
- Note: Blood ammonia is ↑ but the ↑ doesn't correlate with clinical status.

DDX: Subdural hematoma, Alcoholic intoxication, Wernick's encephalopathy

Precipitant factors

1. GI bleeding (100 mL = 14–20 g of protein)
2. Constipation
3. High-protein meal
4. CNS depressant drugs (e.g., benzodiazepines and barbiturates)

Treatment

- Remove precipitants. Reduce blood ammonia by decreasing protein intake
- Lactulose oral (converts NH3 to unabsorbed NH4, produces diarrhea, alters bowel flora). In coma, it is give as enema.
- In refractory cases, add neomycin, metronidazole, or vancomycin.
- Liver transplantation if indicated.

ASCITES

Definition: Accumulation of fluid within the peritoneal cavity.

Causes (DDx)

1. Cirrhosis
2. CHF
3. Nephrotic syndrome
4. Infections [Bacterial OR Tuberculosis]
5. Malignancy

Others: Myxedema, CTD, Pancreatitis, Budd-Chiari syndrome, Meigs syndrome.

Symptom

- Small amounts may be asymptomatic.
- Large amounts cause abdominal distention and discomfort, anorexia, nausea, early satiety, heartburn, flank pain, and respiratory distress.

Examination

Fullness of flanks, umbilicus flat or everted.

Difference between Ascites and Fatty distension	
Ascites	Fatty distension
Distension of the flanks Umbilicus flat or everted	Distension is central Umbilicus is inverted

Degree of ascites:

- Minimal → Dullness only in Knee-elbow position
- Moderate [1-2 L] → Shifting dullness positive
- Tense (severe) [2-4 L] → Transmitted thrill

Note: At least 1 liter of fluid is accumulated to have signs of ascites

Investigations

- **Ultrasound.**
- **Diagnostic paracentesis** (50–100 mL): Routine evaluation includes:
  - Inspection [Bloody → malignancy, Cloudy → bacteria]
  - Biochemistry: Albumin, Glucose, Amylase
  - Gram's and Acid-fast stains, culture
  - Cytology WBC count with differential

Pathophysiologic classification using serum ascites albumin gradient:

Difference in albumin concentrations between serum & ascites:

- *Low gradient* (serum-ascites albumin gradient <1.1): Bacterial peritonitis, neoplasm, pancreatitis, nephrotic syndrome.
- *High gradient* (serum-ascites albumin gradient > 1.1): suggests ascites is due to Cirrhosis, Portal hypertension, CHF, Budd-Chiari syndrome.

Pathophysiology of cirrhotic ascites:

1. Portal hypertension
2. Hypoalbuminemia
3. Hepatic lymph retention
4. Renal sodium retention: due to hyperaldosteronism (aldesterone is normally metabolized by the liver)

Treatment

- Monitor weight, and serum electrolytes.

1. Rigid salt restriction (400 mg Na/d).
2. Fluid restriction of 1–1.5 L only done if pt has hyponatremia.
3. Diuretics → Spironolactone is the drug of choice [aldosterone-antagonist)
   → Furosemide may be added if necessary.
4. Large-volume paracentesis up to 5 L/day with IV infusions of albumin (10 g/L ascites removed). It may be used in:
   i. Initial treatment because of lesser side effects than diuretics
   ii. Refractory ascites [not responding to diuretics]
5. In refractory cases consider transjugular intrahepatic portosystemic shunt [TIPS]
6. Consider liver transplantation.

Prognosis: 50% die within 2 years, and only 20% live for 5 years.

Hepatocellular carcinoma

Epidemiology: M>F. Age- 40-60 yrs.

Risk factors

- Hepatitis B and C [it's the major risk factor]
- Cirrhosis: alcohol, hemochromatosis, primary biliary cirrhosis
- α-1 antitrypsin deficiency
- Glycogen storage disease
- Drugs: CCP, anabolic steroids
- Hereditary tyrosinosis
- Aflatoxin
- Porphyria cutanea tarda

Clinical picture:

- Fatigue, Anorexia, Weight loss.
- Abdominal pain and ascites.
- On examination pt has hepatomegaly with hepatic bruit

Investigations:

- Alpha-fetoprotein (AFP) is +ve in 60% of pts with liver carcinomas "primary or secondary", other causes of raised α-fetoprotein are HBV and HCV infection.
- US can detect lesion > 3 cm, CT scan & MRI are better
- Screening: in pts with high risk is done every 6-months with AFP & US

Treatment

- Liver resection or transplantation

Pancreatitis

	ACUTE PANCREATITIS	CHRONIC PANCREATITIS
Mechanism	Leakage of pancreatic enzymes into pancreatic & peripancreatic tissue.	**Irreversible** parenchymal destruction → pancreatic dysfunction.
Risk factors	[GET SMASHED] **G**allstones **E**thanol **T**rauma **S**teroids **M**umps, Coxsackie B **A**utoimmune, **A**scaris **S**corpion venom **H**yperlipidemia **H**ypercalcaemia **H**ypothermia **E**RCP **D**rugs (Azathioprine, Corticosteroids, Mesalazine, Thiazide, Frusemide, Na-valproate) **Gallstones** the most common cause	• **Alcoholism** (80%) most common cause • Gallstones • Hyperparathyroidism [↑Ca^{++}] • Pancreas divisum. • Idiopathic.
Clinical Picture	Severe epigastric pain (radiating to the back) relieved by leaning forward, nausea, vomiting, weakness, fever, ascites, shock. If hemorrhagic pancreatitis: **Grey Turner sign**: purplish coloration of flank **Cullen's sign** periumbilical discoloration	Triad: **1. Chronic persistent epigastric pain** **2. Steatorrhea** **3. DM** [after 20yrs when >90% pancreas damaged] Other features include: anorexia, nausea, constipation, flatulence. Pain ↓ by alcohol or leaning forward.
Investigation	• ↑ amylase, ↑ lipase [Lipase is more specific] • ↓ calcium if severe •AXR "sentinel loop" or "colon cutoff" sign • CT scan is better than US may show hemorrhage, necrosis, or pseudocyst.	• Fecal elastase to detect exocrine failure • ↑ or normal amylase and lipase • FBS for DM • AXR → pancreatic calcifications • CT ("chain of lakes")
Treatment	Supportive measures: Pain killer [opiates but avoid morphine because it → spasm in sphincter of Oddi] IV fluids/electrolyte replacement Analgesia Bowel rest: [NGT, NPO] Nutritional support IV antibiotics, respiratory support, & surgical debridement if necrotizing pancreatitis.	Exogenous lipase/trypsin and Medium-chain fatty-acid diet. Stop Alcohol For the pain: • Analgesia • Celiac nerve block • Surgery
Complication	Pancreatic pseudocyst (characterized by persistence of ↑ amylase) Fistula formation, Abscess Hypocalcemia Renal failure, pleural effusion, splenic vein thrombosis, chronic pancreatitis, sepsis.	Chronic pain (⅓ of pts ch. opiate users) Malnutrition/weight loss is common because pain ↑ with eating. Pancreatic cancer. Portal or splenic vein thrombosis Peptic ulcer, obstructive jaundice.

Ranson's Criteria for Acute Pancreatitis	
ON ADMISSION	AFTER 48 HOURS
"GA LAW": • Glucose > 200 mg/dL • Age > 55 years • LDH > 350 IU/L • AST > 250 IU/dL • WBC > 16,000/mL	"C HOBBS": • Ca2+ < 8.0 mg/dL • Hematocrit decrease by > 10% • O_2 PaO_2 < 60 mmHg • Base excess > 4 mEq/L • BUN increase > 5 mg/dL • Sequestered fluid > 6 L
The risk of mortality is 20% with 3–4 signs, 40% with 5–6 signs, and 100% with ≥ 7 signs.	

(46)

Hematology

Hematological values		
Index		Range
White blood cell (WBC)		4-11 x10⁹/l
Differential WBC count	Neutrophil	2-7.5 x10⁹/l
	Lymphocytes	1.5-4 x10⁹/l
	Eosinophils	0.04-0.4 x10⁹/l
	Monocytes	0.2-0.8 x10⁹/l
	Basophils	< 0.1 x10⁹/l
Red blood cells (RBC)		
	Male	4.5-6.5 x10⁹/l
	Female	3.8-5.8 x10⁹/l
Hemoglobin: male		130-170 g/l (13-17 g/dl)
Hemoglobin: female		120-160 g/l (12-16 g/dl)
Hematocrit = Packed cell volume (PCV)		
	Male	40-54%
	Female	37-47%
Mean cell volume (MCV)		80-100 fl
Mean cell hemoglobin (MCH)		27-32 pg
Mean cellular hemoglobin concentration (MCHC)		31-35 g/dl
Red cell distribution width (RDW)		11.5-15
Platelets		150-400 x10⁹/l
Erythrocyte sedimentation rate (ESR)		
	Male	<10 mm/hr
	Female	<15 mm/hr
Coagulation tests		
Bleeding time		< 8 mins
Prothrombin time (PT)		12-16 sec.
Activated partial thromboplastin time (APTT)		21-27.5 sec.
Fibrinogen		2.4-4 g/l
Fibrin degradation product (FDP) (D-dimer)		< 0.5 mg/l

Values that you should know are shaded

Abdominal Examination checklist

Action	YES	NO	Action	YES	NO
Permission taken			Percuss for liver span		
Stood on the Right side of bed			Palpate for spleen		
Adequate Exposure			Palpate spleen in Rt lat position		
Position the patient			Palpate for renal enlargement		
Inspection			Check hernial orifices		
Stand at the end of the bed			**Percussion**		
5 S			Shifting dullness		
Stria			Fluid thrill		
Scratch marks			**Auscultation**		
Movement with respiration			Warm stethoscope		
Umbilicus			For Intestinal movement		
Palpation			For bruit if hepatomegaly		
Ask the pt if there is pain			For venous hum		
Kneel down + Warm hands			**I would like to** Ex genitalia and do DRE.		
Do superficial palpation			**Ethics**		
Do deep palpation			Dress the patient back		
Eyes kept on pt face			Thank the patient		
Palpate for the liver					

Abdominal Examination

Preparation

- Permission
- Ensure the patient is lying flat (remove any extra pillows, if present, with the permission of the patient); the hands should lie by the patient's side with the
- Exposure: Abdomen exposed from the inframammary region to just above the genitalia. Do not expose the genitalia.

Inspection

- Symmetrical or not
- Swelling = Distention: Fat, Fluid, Flatus, Feces, Fetus

Difference between Ascites and Fatty distension	
Ascites	Fatty distension
Distension of the flanks	Distension is central
Umbilicus flat or everted	**Umbilicus** is inverted

Ascites grades:

Minimal → Dullness only in Knee-elbow position
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Tense (severe) → Transmitted thrill